TWENTY-FIRST ANNUAL MEETING

OF THE

AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION

HELD AT THE

HOTEL TRAYMORE, ATLANTIC CITY, N. J.

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CONSTITUTION AND BY-LAWS

OF THE

AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION.

CONSTITUTION.

ARTICLE 1. This Association shall be known as the American Gastro-Enterological Association.

ARTICLE 2. The object of this Association shall be the promotion of investigation of the normal and pathological conditions of the digestive organs.

ARTICLE 3. Membership in this Association shall be of three kinds: (*a*) Honorary, (*b*) Corresponding, (*c*) Active.

(*a*) Honorary membership shall be restricted to such as have attained an international reputation by their published works and have scientifically furthered the subject of gastro-enterology. Their nomination shall take place at the annual meeting, upon the written suggestion of at least six active members and on the recommendation of the Council of the Association at the next annual meeting. Their election shall be by unanimous vote of the members present.

(*b*) Corresponding membership shall be restricted to foreign scientists in recognition of meritorious work within the scope of the Association. Candidates for such membership shall be proposed by at least six active members and receive the recommendation of the Council at the next annual meeting. Their election shall be by unanimous vote of the members present.

(*c*) Active membership shall be restricted to American and Canadian investigators and practitioners who have published meritorious work in normal or pathological anatomy or physiology, in medicine or surgery of the digestive canal and its secretory appendages, and who enjoy an unimpeachable moral standing in the medical profession.

Names of candidates for active membership must be: (1) Proposed by two active members who are not members of the Council, such proposal to be submitted to the Committee on Admissions and Ethics, which should report to the Council as soon as possible; (2) Must be recommended by the Council and (3) must receive a majority of the votes of active members present at the annual meeting of the Association.

The election of active members shall take place at the annual meeting of the Association and shall be by ballot.

It shall be the duty of the Secretary to notify active members of all nominations that are to be submitted to the Association at the annual meeting.

ARTICLE 4. The officers of the Association shall be a President, two Vice-Presidents, a Secretary and Treasurer, the latter two offices being vested in one; also three specially chosen active members to be known as Councilors, who, together with the officers, shall constitute the Council of the Association. The said Councilors shall be elected as follows: one for one year, one for two years, and one for three years.

ARTICLE 5. There shall be a Committee on Admissions and Ethics. It shall consist of the President and the Secretary and three other members, not members of the Council. These members shall be elected at the annual meeting at which this Amendment shall be adopted for the following terms: one for three years, one for two years and one for one year. At each subsequent annual meeting one member shall be elected for the term of three years to fill the annual vacancy. No member of the Committee shall be eligible for re-election until after one year shall have elapsed from the end of his term of service. It shall be the duties of the Committee on Admissions and Ethics to examine the merits of a candidate, to investigate any charges made against a member, and to report the results of the examinations and investigations to the Council in writing in the shortest possible time. It shall also be the duty of this committee to study the active work in science and practice of gastro-enterology accomplished in this country and Canada and to invite the meritorious workers to join this Association.

ARTICLE 6. The election of officers, Councilors and of the members of the Committee on Admissions and Ethics shall take place at the annual meeting and shall be by ballot.

ARTICLE 7. Vacancies in the offices occurring in the interval between the annual sessions shall be filled temporarily by the Council.

ARTICLE 8. The annual meeting of the Association shall be held at a time and place to be decided by the Council.

ARTICLE 9. The President shall be the chairman of the Council.

ARTICLE 10. There shall be annually two meetings of the Council; one shall take place at the call of the President, shortly after the annual meeting of the Association; the other shall take place at least four weeks previous to the annual meeting. It shall be within the discretion of the President to conduct this latter meeting by correspondence.

ARTICLE 11. The Council shall manage the affairs of the Association in accordance with the Constitution and By-Laws, and its minutes shall be reported to the Association at the annual meeting.

ARTICLE 12. This Constitution may be amended by a two-thirds vote of all the active members at any annual meeting, provided that notice of proposed amendments has been given in writing to all the

active members of the Association by the Secretary, and provided further that such proposed amendments shall have been submitted to the Council and held over for one year.

ARTICLE 13. Any member failing to attend three consecutive annual meetings without an excuse acceptable to the Council shall be dropped from the roll. The Secretary, however, shall be required to call the attention of a delinquent member to the facts in his case previous to the third meeting.

ARTICLE 14. This Association adopts the Code of Ethics of the American Medical Association. Charges of advertising, of publishing knowingly false scientific statements, of actions unbecoming a gentleman and a high standing physician, etc., shall be investigated by the Committee on Admissions and Ethics. The accused shall have liberal opportunities to clear himself of the accusation. The Committee shall report its findings to the Council, and on the recommendation of this body an offending member may be expelled by a three-fourths vote of those present at the annual meeting.

BY-LAWS.

ARTICLE 1. The President and Vice-President shall discharge such duties as are implied by their respective offices. The President shall preside at all sessions of both Council and Association.

ARTICLE 2. The Secretary shall attend to the usual clerical duties of the Council and Association. As Treasurer, he shall keep a record of the payments and arrearages of dues, and report on both at the annual meeting.

ARTICLE 3. The Council shall report its transactions to the annual meeting of the Association. It shall superintend the publication of scientific papers, but shall not appropriate for such printing an amount exceeding the sum of $100, without the vote of the Association. The order of business shall be arranged by the Council before the annual meeting. It shall pass upon the eligibility of candidates for membership.

ARTICLE 4. The yearly dues of active members shall be five dollars, payable in advance. Any member whose subscription shall be in arrears more than two years shall be reminded of the fact by the Treasurer, in writing in event that payment be not then made he may, on vote of the Council, be dropped from the roll of the Association. It shall be the duty of the Treasurer to report all members who are in arrears to the Council.

ARTICLE 5. When sufficient money is in the treasury the membership dues may be omitted when decided by the Council.

ARTICLE 6. These By-Laws may be amended, repealed or suspended by a two-thirds vote of the members present at any meeting of the Association.

ARTICLE 7. The quorum of the Association for the transaction of business, but not for the reading of papers, shall consist of seven active members.

ARTICLE 8. All titles of papers submitted for reading at the annual meeting shall be sent to the Secretary not later than four weeks before the date of the meeting.

ARTICLE 9. A typewritten abstract of not over three hundred words, of every paper to be read, must be sent to the Secretary at least four weeks before the annual meeting. It shall be the duty of the Secretary to send to each member of the Association a complete list of the papers to be read at the annual meeting, with their full titles, at least two weeks before the annual meeting.

ARTICLE 10. Papers submitted to be read before the Association shall not have been previously published or read elsewhere. Papers shall not exceed the limit of fifteen minutes without the consent of the majority of members attending.

PRESIDENT'S ADDRESS

To the members of the American Gastro-Enterological Association, invited guests, ladies and gentlemen:

Before proceeding with the few remarks which will constitute the fulfillment in part of the obligation of the high office to which your association has seen fit to appoint me, I wish to thank you for the honor conferred upon me. This honor came to me unsought and was the farthest from my expectations. From year to year as we have met and the nominating committees have designated our successive presidents, I have recognized their strong qualifications, and their peculiar fitness for the various developments and crises which have occurred in the eventful history of this association. It would afford me great pleasure at this time to speak of the successive events of the past twenty-one years' existence of our association, and of the determining guidance and inspiration which each one of my worthy predecessors has, from year to year, brought to us; but there are several reasons which forbid my entering into such happy and pleasing reminiscences.

The first and most important is that in these stirring times when history is being made rather than chronicled it is scarcely fitting to look back and speak of things which have been brought to pass, however important they may have been; it is rather more fitting to speak of the things which are before us and with which we are here and now confronted. We feel our obligations individually in this great world struggle, but as an association we should feel them collectively. The program of today and tomorrow will, I hope, bring out such discussions of such vital things in our special work pertaining to the success of our arms as will make this the most notable meeting in the history of the association. They say food will win this war. That means not only that there must be a superior knowledge of the production, preserving, storing, and transportation of food, but there must be a superior knowledge of the value and adaptation of food to the body subjected to varying conditions and circumstances.

What organization can furnish such knowledge better than ours? A number of our members are already in the M. R. C.,

but what are we who have been left behind doing? Are we doing all we can and should do?

The highest point of service which one can reach individually is to offer himself unreservedly for immediate military duty. Possibly more of our number could do this. Collectively we can do possibly even more or a service which will accomplish greater results. Our chiefs, Gorgas, Braestead and Blue, heads of the various departments in this great war are in need of medical men, in need of encouragement and frequently seek advice. They need to get in touch frequently with organizations who can supply these needs. I would suggest that this association through a perfectly constituted committee offer its services in the directions suggested, and that at this meeting definite action be taken again to show that we are ready to serve.

I leave these questions with you while I go on to discuss a few observations which have come to me with considerable emphasis during recent years. I refer to

The Relative Incidence of Peptic Ulcer of the Duodenum and of Carcinoma of the Duodenum.

In this discussion I do not wish to refer so much to the development of our knowledge in regard to these two lesions in the duodenum, but rather to call your attention, on the one hand, to the present acknowledged frequency of duodenal ulcer and, on the other hand, to the infrequency of cancer in this same region.

It is interesting, however, to note that cancer of the duodenum was first described by Hamburger as early as 1746, since which time the lesion has been found only occasionally. Ulcer of the duodenum was first mentioned in medical literature in 1817. In 1830 it was possible to collect only five cases from the literature, and in 1894—only 25 years ago—a thesis by Collin (Paris) contained a summary of 257 cases recorded to that time, and notes of additional five cases observed by him. At present almost any clinician who sees a considerable number of gastro-intestinal diseases is able to number his duodenal ulcer cases by the hundreds. It is interesting to note, therefore, that while carcinoma of the duodenum has been known for almost two centuries, it is now seen scarcely more frequently than when it was first described. Of 808 cases of cancer of the intestine collected by Nothnagel, and others, only 42, or 4.5 per cent., were of the duodenum;

and of cancers in general, statistics show that only about 0.34 per cent. occur in the duodenum.

Ulcer of the duodenum, popularly known, we might say, for only twenty-five years, is now the most frequently recognized lesion in the gastro-intestinal canal—even more frequently than ulcer of the stomach. This was first shown by the Mayos and has since been confirmed by many other observers.

In reviewing my own cases I have found but six cases of carcinoma of the duodenum, and about 240 cases of carcinoma of the stomach—a ratio of one to forty. The diagnoses gastric carcinoma have largely been verified by autopsy or operation. When neither autopsy or operation was done the diagnosis was confirmed by the inevitable course of all cancer cases. The six cases of cancer of the duodenum were all verified by operation or autopsy, with the exception of one in which autopsy was not permitted. The diagnoses in all the cancer cases are, therefore, reasonably certain.

Reviewing over 1,000 cases of peptic ulcer, collected during the same period in which the cancer cases were collected, I find a diagnosis of ulcer of the duodenum 480 times whereas ulcer of the stomach was diagnosed 540 times. While in these statistics one cannot feel so certain of the diagnosis of peptic ulcer, and especially as to whether in the stomach or duodenum, as of the diagnosis of carcinoma the figures have some significance. It may be inquired why ulcer of the stomach was reported slightly more frequently than ulcer of the duodenum since nearly all clinicians agree that just the opposite is the case. In my earlier work X-ray examinations and string tests were not available or even known and it was difficult to make the diagnosis of the presence of an ulcer, not to speak of its definite location. It was only after visiting the Mayo Clinic as well as Sir Barclay Moynihan's Clinic, some ten years ago, that I appreciated the fact that duodenal ulcer does occur and that many of my so-called hyperchlorhydrias, which formerly had been considered as cases of gastric neurosis or gastric ulcer were cases of duodenal ulcer. Since then, with more careful histories and with the aid of the X-ray, the Einhorn string test, and other proceedings, the diagnosis of duodenal ulcer has been made more frequently, and probably now two out of three cases of peptic ulcer are found in the duodenum.

My experience in this is not unique, for in 1904 the relation of recognized gastric ulcer to ulcer of the duodenum was:

	Gastric Ulcer 73%,	Duodenal Ulcer 27%
In 1907.....	Gastric Ulcer 52%,	Duodenal Ulcer 48%
In 1910.....	Gastric Ulcer 35%,	Duodenal Ulcer 65%
In 1914.....	Gastric Ulcer 27%,	Duodenal Ulcer 73%

Though my ulcer statistics may not be so reliable as the cancer statistics, they show that duodenal ulcer occurs at least as frequently as gastric ulcer and that there is not the same discrepancy, one to forty, as there is in carcinoma in these two divisions of the gastro-intestinal tract.

Another interesting observation of this study was the location of carcinoma in the duodenum. It is a well-known and recognized fact that carcinoma in the stomach is distributed in relative frequency to various parts of the stomach about the same as peptic ulcer. In other words, the location of gastric cancer corresponds rather strikingly to that of gastric ulcer. In the duodenum, according to reports found in the literature and according to my own reports, this similar distribution does not occur. According to Moynihan at least 95 per cent. of peptic ulcers lie in the first portion of the duodenum or within one and a half inches of the pylorus. The further the distance from the pylorus the less frequently is ulcer found. It is unusual to find an ulcer near or about the papilla of Vater.

It is possible to find but few satisfactory reports in the literature of cases of carcinoma of the duodenum located exactly in the most frequent ulcer bearing area, *i. e.*, within the first one and a half inches of the gut. Most reports seem to be of growths which come direct from the pyloric ring or immediately from or about the papilla of Vater. This fact is confirmed very strikingly in the six cases of cancer of the duodenum which I shall report. None were found in that area which is most frequently the seat of peptic ulcer: before the excision two were thought to be in this area, but were shown by the pathologist to have arisen from the pyloric ring and simply dipped down into the first portion of the duodenum; three others were shown to have come from and about the ampulla of Vater; and the sixth, which was not operated or autopsied, corresponded so closely and definitely

in history, symptoms and clinical findings to the other cases of carcinoma of the ampulla that it was included.

In reporting these cases I shall refer only to the autopsy findings, or to the observations in the operating room, as it is the pathology only which concerns us in this presentation.

CASE I.—Mr. H. A. F., aged 42; February, 1910, was operated upon for a pyloric stenosis due to a carcinoma. The pylorus, with the first portion of the duodenum, was resected. It was thought during the operation that the carcinoma had its origin in the first portion of the duodenum, but the pathologist, Dr. Klotz, demonstrated definitely that the growth came from the pyloric ring.

CASE II.—Mrs. J. D. C., age 62; October, 1910, was operated upon for gall stones and possible carcinoma of the gall-bladder. Forty gall stones were found, one impacted in the common duct which was enormously distended. On account of the extensive infection the patient died several weeks after the operation. Autopsy performed by Drs. Klotz and Hathorn showed "a carcinoma involving the duodenum at the entrance of the bile and pancreatic ducts. The condition was complicated by gall stones causing stagnation of the bile in the ducts and in the liver, while the pancreatic fluids distended the pancreatic duct to the formation of cysts."

CASE III.—Mr. E. H. A., age 56; March, 1911, was operated upon for pyloric stenosis, possibly malignant. A tumor as large as an English walnut lay in the first portion of the duodenum having its origin, seemingly, in the pyloric ring. A gastro enterostomy was done. Five months later the patient died. An autopsy was not permitted and, therefore, this case may be somewhat in doubt.

CASE IV.—Mrs. E. C., age 67; May, 1916, was operated upon for empyaema of the gall-bladder and possible stone in the common duct. Pus was found in the gall-bladder. The common duct was obstructed not permitting a probe to pass into the duodenum. At the autopsy a carcinoma was found at the papilla.

CASE V.—Mr. N. J. H., age 57; May, 1917, was intensely jaundiced and septic. Died two weeks after entering the hospital. At the autopsy a primary carcinoma of the ampulla was found, the proximal side of the papilla having been destroyed by the growth.

CASE VI.—Mr. C. L. M., age 68. This case should probably not be included in this list, but the symptoms were identical with those of Case V and the physical findings were the same. Gastric analysis was free Hcl 0, combined 6, and total 12, no blood and lactic acid. A silk string was blood stained in the bile stain. Operation was refused. The patient died in two months and no autopsy was permitted.

In summing up this data it appears—

First.—In a series of 486 patients with duodenal lesions six

were found to be cancerous and 480 were benign ulcers—a ratio of one to eighty.

Second.—In a series of 780 patients with gastric lesions, 240 were found to be cancerous and 540 were benign—a ratio of one to two and a fourth.

Third.—In the duodenum the cancer usually had its origin either in the pyloric ring (twice) or at the papilla of Vater (four times), whereas, according to Moynihan, 90 per cent. of the ulcers are in the first one and one half inches of the duodenum. Apparently, then, the cancer bearing areas and the ulcer bearing areas do not coincide in the duodenum as they do in the stomach.

From these facts we must necessarily conclude that in as much as duodenal ulcer is more frequent than gastric ulcer, and duodenal cancer decidedly less frequent than gastric cancer, and in as much as the distribution of the two lesions coincides in the stomach, but does not coincide in the duodenum, it would appear highly improbable that peptic ulcer is an etiological and determining factor in carcinoma of the stomach. Or, to express the matter in the form of a question. If carcinoma of the stomach arises so frequently (50 to 70 per cent., according to some) from a peptic ulcer, why doesn't carcinoma occur more frequently in the duodenum where peptic ulcer abounds? Is it not probable that the etiological and determining factor of carcinoma of the stomach is something entirely independent of peptic ulcer? These are questions which come to the clinician and appear difficult to answer. It may be that the anatomist or the physiologist or the biological chemist has a ready and satisfactory answer.

THE PSYCHIC ELEMENT AS AN IMPORTANT FACTOR IN THE DEVELOPMENT AND TREATMENT OF PEPTIC ULCER.*

By Jacob Kaufmann, M. D.,

NEW YORK.

A rational and successful treatment of peptic ulcer may be expected only when we are able to clear up and eventually eliminate those causative factors which, in a given case, provoked the ulcer.

Clinical observations have convinced me that in different cases different factors come into consideration, either more or less combined or with one cause as the principal one.

Today I wish to single out for discussion the fact that in one group psychic influences; great emotional display, nervous shock, unduly prolonged or intense mental strain, and over-exertion play a prominent causative role in the development of the ulcer.

As a rule we are dealing here with high-strung, excitable individuals who are prone to indulge in over-activity. Not infrequently they are strongly built, energetic people who lead a very active life in many respects, and in whose histories we find that periods of mental or emotional excess regularly precede the periods of gastric suffering and ulcer symptoms. In the histories of other cases the mental exertion and the emotional strain do not stand out so prominently as unduly great, but they are relatively so for the given individual. It often happens that smaller psychic annoyances, over a certain period of time, cause only a milder form of gastric disturbance until the advent of some greater psychic taxation acutely aggravates the condition, provoking pain and other signs of more severe gastric irritation, eventually leading up to the fully developed ulcer picture.

When we take the trouble to inquire into the mode of living of our patients, we can hardly overlook the fact that a causal relationship exists between psychic activity and peptic ulcer formation.

*Read before The American Gastro-Enterological Association, Atlantic City, May 6th, 1918.

Not so obvious, however, is the mechanism of this causal relation and we enter upon unsafe grounds when we try to explain its working. I shall not venture too far into theoretical fields, but shall restrict myself to the brief sketch of some considerations which may, possibly, yield the basis for an explanation.

The intimate connection between the mental states and digestive activity and its disturbances, long known to the laity as well as to medical observers, was experimentally demonstrated by Bidder and Schmidt, Schiff, and later more extensively by Pawlow, Bickel, Cannon, and others. For our question I refer especially to the part of Cannon's work which deals with the influence of emotional states on adrenalin secretion and the influence of adrenalin on the activity of the alimentary tract.

Attempts have been made to correlate the effect of adrenalin on the function of stomach and duodenum, with peptic ulcer formation. Some investigators succeeded in producing gastric and duodenal ulcer in animals by repeated injections of adrenalin, while others achieved the same result by adrenalectomy.* Clinically it may be pointed out, that the type of duodenal ulcer which is observed after extensive burning of the skin, may be the result of the destruction of a great part of the chromaffin system in the burned area.

However, not only the adrenals get disturbed by psychic irritation, but with their intimate inter-relation, other endocrine glands get involved, especially the thyroid. Experimental research also records the finding of ulcerations in the stomach and duodenum after partial thyroidectomy. I quote these experiments to indicate the trend of opinion of investigators who try to show that dysfunction of the endocrine glands may create the basic conditions for the formation of ulcers.

In speaking of the endocrine function we should bear in mind that it is closely interlinked with the function of the vegetative nervous system, the tone of which on the one hand is said to depend upon the secretion of the endocrine glands, while on the other hand the activity of the endocrine glands is regulated through stimulation by the vegetative nervous system.

It must be admitted that there is still a scarcity of facts which

*For literature and discussion of the topic see A. G. Friedman, Arch. of Diagnosis, January, 1917.

would support the theoretical claims by demonstrating that internal secretion disorders and the correlate derangement of the vagus and sympathetic nervous system may be responsible for such functional disturbances as spasm, increased secretions of gastric juice with diminished amounts of mucus* which we consider essential elements in the pathogenesis of peptic ulcer.

Furthermore, before we can fully utilize this conception in explaining the causative role of psychic influences, other problems will have to be solved, for example, the question why the same emotional and mental upsets provoke in one patient peptic ulcer, in another bilious attacks, in a third bronchial asthma, in a fourth arterial hypertension, in a fifth Graves' disease, and so forth. It seems that the examination of constitutional characteristics and anomalies, which has lately been greatly stimulated by the study of endocrinology, is throwing a good deal of light upon this intricate question. Without taking up the discussion of this topic we may say, in a general way, what the combined disorders of the endocrine function and of the vegetative nervous system, when provoked by psychic irritation, in individuals of a certain type or under certain conditions, react particularly on stomach and duodenum. This reaction, which manifests itself in spasm and secretory disturbances, may produce erosions. I would like to emphasize, that it is the frequent repetition of the reaction which gradually changes the growing initial, anatomical lesion of an erosion into an ulcer, and which finally accounts for the chronicity of the ulcer.

While we may leave it to future investigators to define more specifically the manner in which psychic influences act in bringing about the formation of peptic ulcer, about one point there can be no doubt and that is, that once the causal relationship is recognized we have to take it into account in laying out a plan of treatment.

Whatever other medical or surgical treatment may be indicated, according to the condition which the case presents, the final result, especially the prevention of recurrences, depends to a high degree on the possibility of eliminating further periods of display of harmful psychic influences. With this object in view,

*J. Kaufmann, Lack of Gastric Mucus and Its Relation to Gastric Ulcer. *American Journal of Medical Sciences*, February, 1908.

we must enlighten the patient on his short-comings, we must advise him to avoid emotional excesses and to redress faulty habits of mental activity. This may involve a thoroughly revised mode of living and eventually necessitate a change of occupation.

One of my patients, a young lawyer, was subject to periodical mild attacks of gastric hyperacidity. While he was trying an important case in court, the gastric disturbance became more and more pronounced as the proceedings drew out over a longer period of time, until one particularly hard day repeated attacks of violent gastric pains occurred, followed by a profuse hematemesis in court. After a strict medical ulcer treatment the patient fully recovered from the severe anemia and since he remained free from subjective symptoms, he forgot the advice given him and a year later again conducted a difficult long drawn out case in court, when he met with the same experience of quickly increased gastric suffering winding up with a profuse hemorrhage. This time the advice held good for two years, when the perfect recovery led him to think that he now could stand up under the strain of a prolonged court trial. The third hemorrhage coming on under the same circumstances finally convinced him; and after abstaining from the exacting and exciting court work and restricting his activity in law to office work he escaped further attacks of severe gastric suffering and bleeding.

It is certainly not always possible for patients to give up an occupation for which they are temperamentally unfit, nor is it an easy task for them to modify their mental and emotional habits. But the difficulty encountered here is not greater than with other diseases, the treatment of which calls for a different mode of living and a change of occupation. With proper direction a good deal can often be accomplished, and when a change is feasible, as in the case quoted, a favorable result may be obtained. On the other hand, experiences have made it clear to me that it is the utter disregard of primary causative factors, such as harmful psychic influences, which accounts in many cases for the frequent recurrences with which we are so familiar in peptic ulcer. This applies not only to patients who are treated medically, but just as much to those who undergo operations.

I have the records of a number of patients who, in spte of several successive gastric operations, had recurrences because in the after treatment no attention whatsoever was paid to the

mental and emotional upsets which, after a more or less extended interval invariably brought on a renewal of the ulcerative process. One of these patients, a highly neurotic trained nurse, had not less than four gastric operations performed for attacks of ulcer symptoms and hemorrhage. When another attack with profuse bleeding occurred, a surgeon proposed a fifth operation which the patient declined. A study of her history showed that she was very ambitious and periodically indulged unreasonably in overwork, gradually getting more and more excited, and that such periods of mental and emotional excess were usually followed by pronounced gastric suffering often associated with hematemesis.

We must realize that operative measures are not essentially causal methods of treatment. Surgery may deal successfully with sequelae of ulcers, with stenosis, perforation and so forth. A gastroenterostomy may prove helpful in combating the ulcerative process by disrupting a vicious circle; but no kind of operative proceeding, not even the complete resection of the ulcer, will prevent recurrences as long as the original causative factors which provoked the formation of the primary ulcer are allowed to come into play again.

As we have seen, psychical elements may form an important and, we may add, a frequent primary cause.

I stated in the beginning that other exciting causes may provoke the development of peptic ulcers. Among these the reflex irritation from diseased abdominal organs is at present over emphasized; while other causes of irritation, for instance, those due to errors in diet, alcohol and tobacco are disregarded to an astonishing degree. Everyone of the various causative factors will have to be taken into account if we wish to secure a more lasting effect than is usually afforded by the customary set methods of medical and surgical treatment.

From my own experiences I have reason to believe that the proper consideration of all causative factors during the initial stages may serve as a prophylactic measure in preventing the full development of the ulcer.

52 East 58th Street.

DISCUSSIONS.

DR. MAX EINHORN, New York City: With reference to Dr. Hemmeter's remarks I also wish to say that I fully agree with Dr. Kaufmann that the psychic state has a great deal to do with the development of

disease in the stomach. I shall mention only the practical side of it. We all know that we find cases of hyperacidity and other conditions, in which the patients really suffer, but in which we cannot assume that there are anatomic lesions. Such instances are found and often operated on, with the result that nothing is discovered. Such cases exist, but if we wait, and these people come back year after year, we ultimately come to the conclusion that there is present an ulcer. It has not been there all the time, because we can prove it; and we find it developing later. We must say that these periods of long suffering, first considered as a neurotic affection, ultimately lead to the development of organic disease. We do not know exactly the cause of the ulcer, but we know that hyperchlorhydria plays a certain role, and to prevent recurrence we must instruct these patients how to proceed—not to smoke much, not to eat highly seasoned foods, etc., as Dr. Kaufmann says. Whether there is at first an erosion, it is difficult to say, and it is also difficult to say at what period was the beginning of the ulcer. But there is no doubt that clinically we deal with psychic manifestations that ultimately lead to the development of disease.

Dr. Max Einhorn, New York City: Dr. Bryant mentioned that case to me. I should like to say that his treatment of the patient is excellent. They all get the best attention. I think that a great many of them tell the truth; but, on the other hand, I am convinced that the cases in which there is a chronic ulcer are unfit for active service, and that the Government should arrange that they should do secretarial work, not combined with camp duty. One who has had an ulcer, when exposed to great exercise, will have a return of the symptoms, and a hemorrhage will occur. Such men should not be sent abroad. That is what I would suggest for the present. People who are in the hospital and stay a long time, where there is a sure ulcer, should not, even when they improve, be put in a position where they have to do active camp duty.

Dr. Arpad G. Gerster, New York City: What I have to commend most in the treatment of this most interesting subject by Dr. Kaufmann is the manner of its presentation, the broad outlook upon the question, both from the purely scientific side, which was accentuated very definitely and very cautiously, also, because our knowledge there seemed rather uncertain, dwelling on the importance of establishing the cause, if such a cause exists; and, second, the detailed attention to disturbing psychic factors in the dietetic treatment. I am still a general practitioner, and am especially interested in and in sympathy with this part of the paper; being convinced of the value and importance of detailed attention to this matter. In practice many of my surgical colleagues apparently disregard these things, placing reliance on the purely mechanical side of treatment. That disregard is to be attributed, I think, to the fact that so many patients who have been operated upon for gastric disturbances with apparent immediate suc-

cess, return to the hospital again and again with relapsing symptoms, because the vicious mode of dietary regime which caused the primary trouble, was resumed after recovery from the operation. Gross evidences of that occur not only in private practice, but in scientifically conducted large hospitals. In New York City, an instance occurred lately, in a female patient, who had been operated on successfully for gastric ulcer, and had had but little disturbance due to the anesthesia. She was a very intelligent woman, by the way, and she found herself compelled to seek discharge from the hospital on the seventh day, or as soon as the stitches were out, because, from the fifth day on, she had been fed on corned beef and carrots. It sounds incredible, but it is a fact. The patients are left to the care of the inexperienced house surgeon who pays no attention to the diet; the nurses still less. Such things are not right. Anyone who takes pains to make inquiries, as I have done in the hospitals with which I am connected, will find what little attention is paid to the diet, will sometimes meet with an incredible disregard of the subject point, with which Dr. Kaufmann's paper has been dealing.

DR. LICHTY: Dr. Kaufmann's paper is now open for discussion.

DR. MARTIN E. REHFUSS, Philadelphia, Pa.: I was much interested in hearing Dr. Kaufmann's presentation regarding the psychic effect on the manifestation of ulcer. Some time ago we were much interested in higher acidities, and the psychic phase of the gastric curve, and the thing we needed was a method for actually demonstrating the psychic secretion. We are all familiar with the experiments of Pawlow, in which sham feeding was given a dog after a gastrostomy, and also with cases in which this operation had been performed in human beings, but this did not give information regarding psychic secretion in health, so we attempted to obtain data in normal individuals. We took a series of men, six in a row, and in front of each of them we placed a beaker containing one hundred grams of steak. We did this in the early morning, and then passed the fractional tube and completely evacuated the residuum. These men were accustomed to intubation, and it had no psychic effect on them. With the tube in their mouths, they were put in front of the steak and compelled to cook it, and at intervals, we completely removed the secretion. After a time, the secretion in response to the sight and odor of food, ceased. We allowed them to chew the steak, but not swallow it, and analyzed the secretion. We found that the secretion was as high as 240 c.c. It averaged 97.2 total acidity, and ran through the digestive curve in 60 to 80 minutes, and it constituted an important factor to be considered in the digestive phase.

We investigated the effect of atropin on the psychic secretion. I reported some of these things before the American Philosophical Society. We found that atropin cut down the acidity and the amount of secretion, but we could never cause a psychic secretion to disappear completely, even when large doses of atropin were given.

We employed the method on an ulcer of the duodenum and obtained 350 c.c., more than in health. There is a whole chapter regarding psychic secretion in disease that must be worked out, and that method was the only one that suggested itself to us. It has certain advantages. These men were perfectly well and had not been operated on, and we were able to remove the last cubic centimeter of secretion.

Dr. Julius Friedenwald, Baltimore, Md.: I was much interested in Dr. Kaufmann's paper, which was certainly excellent. I want especially to call attention to a fact that I have noted for a great many years in the treatment of ulcer, and that is the psychic element. I am glad that Dr. Kaufmann has called attention to this, for there can be no doubt that it plays an important role. I have found that if a patient is put under favorable influences, and has the rest and freedom from excitement and work, which are the important factors of a good rest-cure, this treatment is more effective than if the patient is not given this special treatment under favorable psychic conditions. Patients are often annoyed very much at hospitals during their course of treatment, and if we properly look into the matter, we often find that this is the cause of the failure in our medical cure. I believe that the notorious failure of ambulatory treatment is largely based on this lack of psychic treatment, which is an important factor in the cure.

Dr. John C. Hemmeter, Baltimore, Md.: With reference to the experiment of Pawlow on the dog with a sham meal, I would say that this has also been done on human beings. You will find in Howell's Physiology a description of a boy with a cicatrical stenosis of the esophagus. In order to feed him, it was necessary to do a gastrostomy. When he saw food or chewed it, the gastric juice came from the canula in the stomach, although no food reached the stomach. The food, of course, could not get into the stomach. That is an exact parallel of the fictitious meal experiment on the dog performed by Pawlow, but it has no bearing on the fact that Dr. Kaufmann wanted to bring home to us. He wanted to emphasize the psychic element as factor of pathogenesis in producing disease. I hope you will be free in discussion, because physiologists in the laboratory experiment almost wholly on animals, and societies like the *Society for Psychic Research* is apt to go too far into metaphysical speculation. Clinical investigation must tell us the facts that are more directly appertaining to man on the physiology of anger and fear. If these conditions can produce pathological states, we should study all of them and with a view to ascertaining as to how far psychic states may be made available, so as to alleviate and cure pathological conditions. As you are aware, an entire religious cult has sprung up on that very basis.

Dr. Jacob Kaufman, New York City, closing: This lively discussion shows that the presentation of the topic was opportune. It was

not my intention to bring before you anything essentially new. The subject is familiar to all who have had experience. On the other hand, there has been too much teaching of late years based exclusively on anatomical features—a purely mechanical conception, as Dr. Garster says, with a disregard of the prevailing, important physiological disturbances. It is just that kind of experience which Dr. Gerster related and which I have had in numerous cases which prompted me to present the paper. I was lately invited to attend a meeting at which the main paper of the evening was on the "Curative Effect of Operations." The essayist thinks that he is able to "cure" peptic ulcer by performing an operation, and after that let the patient do as he pleased, eat whatever he wished. This erroneous conception causes frequent recurrences. No matter what method of treatment you employ, unless you succeed in dealing successfully with the real causal factors, you do not get a lasting result.

The report of Dr. Rehfuss is interesting, corroborating the effect of psychic influence on digestion. Regarding the effect of psychic influence, we must take into account the constitutional make-up. As Dr. Bryant pointed out, it is the constitutional make-up that wants to be considered in connection with the influences of life.

DR. FRANK SMITHIES, Chicago, Ill.: Consciously or unconsciously, I think that Dr. Kaufmann has written one of the most valuable war papers that will be read at this session. We members of the Medical Advisory Boards are instructed that individuals who have symptoms of peptic ulcer shall be sent to cantonments as cases with remediable defects. Those with experience with large numbers of drafted men know that since the draft went into effect, we have had a large number of neurasthentic individuals come with the so-called hyperacidity syndrome or actual gastric ulcer. There have been a great many who have come to my clinic, and many have been referred to me from the Medical Advisory Boards. It is presumed that at the cantonment these patients can secure proper treatment. Anyone who has visited large establishments of this kind knows, however, that frequently the environment is not favorable for restoring normal equanimity. These individuals may remain in the cantonments for a long time, at great expense to the Government, and then, at the end, have to be discharged as not fit for active service. It seems to me that this society should take some action, through Dr. Seale Harris or some other responsible officer with respect to looking to a modification of Medical Advisory Board Instructions. Such would be a tremendous saving to the Government and the medical military side of any large cantonment, and possibly would even save life. We should classify these ulcer individuals for duty in a limited or clerical capacity.

CAPTAIN JOHN BRYANT, M. D., Boston, Mass.: I have had some experience with some of these people that Dr. Kaufmann has been talking of, cases of the less severe grade, in which there has been

supposed to be an ulcer present, but nothing definite has been found on laboratory investigation. I have had a number referred to me, and have had pretty good luck in straightening them out on the lines mentioned, going into the details of their lives and showing them how to live with decreased strain; also adding definite physical reconstruction in the way of neuro-muscular re-education, thus more nearly balancing the expenditure of energy from the nervous system by the increased supply of muscular energy.

Captain John Bryant, M. D., Boston, Mass.: I wish to say another word about the military end of the subject, if I may. It is a question partly of the reaction between the resistance of the individual and the amount of strain to be put on him. A considerable number of these people will improve under the burdens of camp life, but it is questionable whether they will stand up under the increased strain when they get to the front. That is particularly so with officers, who are more subject to these conditions than privates, having more mental responsibility.

I wish to mention one case that I had, in a lieutenant, who had had very hard sieges of mental strain during his life. He came to the hospital with what he said himself was gastric ulcer. He had violent gastric pain, and was perfectly certain that he had ulcers. X-ray examination did not show anything, and I felt sure that the fatigue element was a large factor. Within a week he was well.

I accidentally got two more cases, that he had been trying my method of treatment on. I do not believe that this officer is fit to go abroad. If he ever works from fifteen to twenty hours a day, he will have to be sent back to the United States at the expense of the Government.

PERFORATION IN CANCER OF THE STOMACH.

By Julius Friedenwald, M. D.,
Professor of Gastro-Enterology,

AND

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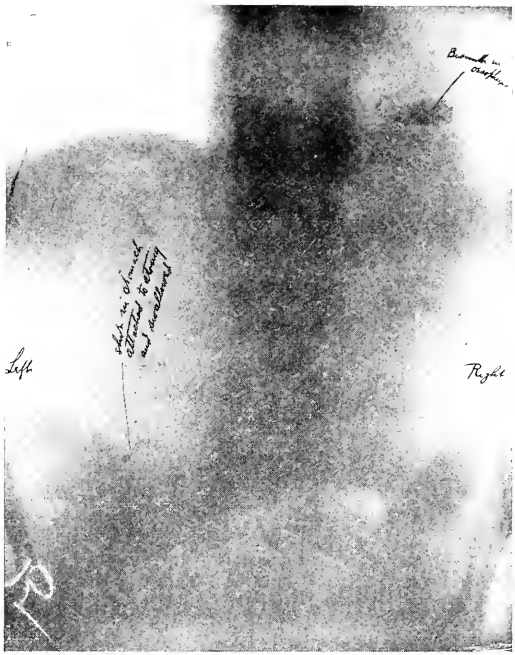
BALTIMORE, MD.

While perforation is a complication often noted in the course of gastric ulcer, and reports on this condition abound in the literature, there are very few reports of a similar complication in the case of gastric cancer.

Brinton's statistics, which are frequently quoted, show 17 perforations into the peritoneum among 507 cases of cancer of the stomach. In this collection there is one case of gastric fistula due to perforation involving the anterior abdominal wall. In the American edition of Riegel's[1] Diseases of the Stomach, edited by Stockton, perforation into the abdomen is classed as a rare termination of cancer of the stomach. W. Hale White in Allbutt's System gives 4 per cent. as the frequency of the complication. Perry and Shaw,[2] made a study of 306 fatal cases of cancer of the stomach collected between 1826 and 1900. There were 13 cases of perforation with acute peritonitis and 7 with localized abscess. Smithies[3] gives 2.5 to 6 per cent. as the frequency of perforation in gastric cancer. In our series[4] of 1,000 cases of cancer of the stomach published in 1914 there were 23 2.3 per cent. presenting signs of perforation, but only in 3 of these cases was the perforation demonstrated.

Perforations of the stomach from any cause may be either acute or chronic. In the first mentioned variety the perforation is accompanied by the urgent symptoms of a spreading peritonitis. With the chronic form there is time for the development of a reaction on the part of the peritoneum, and by organization of the exudated lymph adhesions bind together adjacent viscera and endothelial surfaces and so wall off the area of infection which occurs.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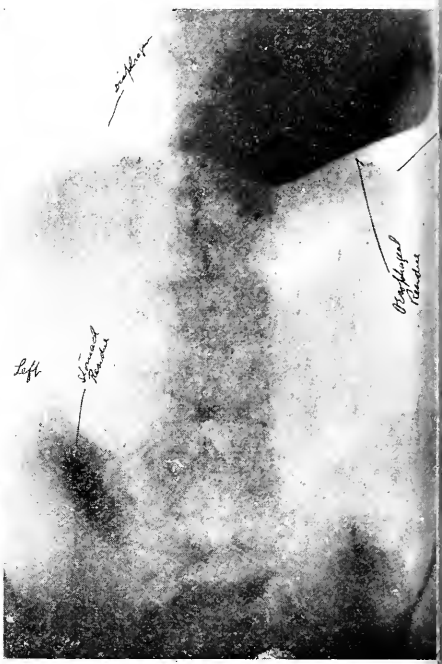
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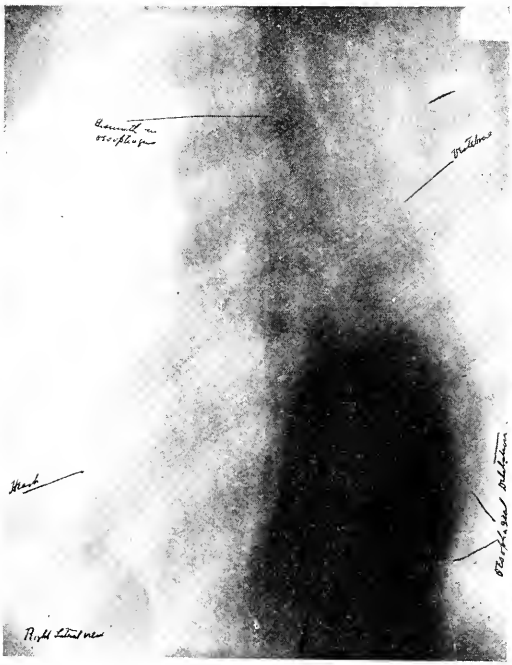
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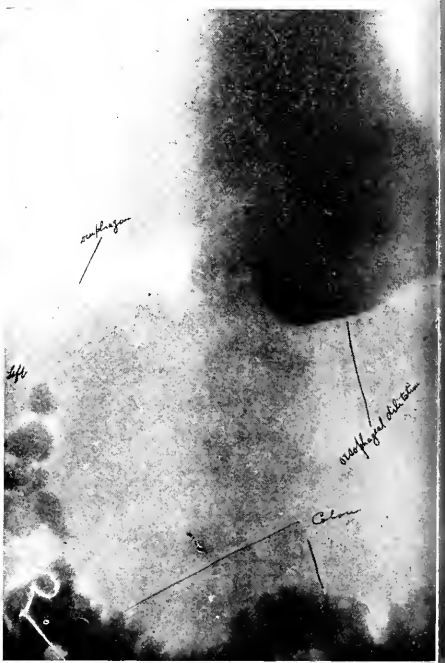
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The dearth of reports on perforated gastric cancer may be explained by the fact that an acute perforation is not often observed, and that the hopeless outlook for cure of the cancer distracts attention from the complication when chronic perforation has occurred.

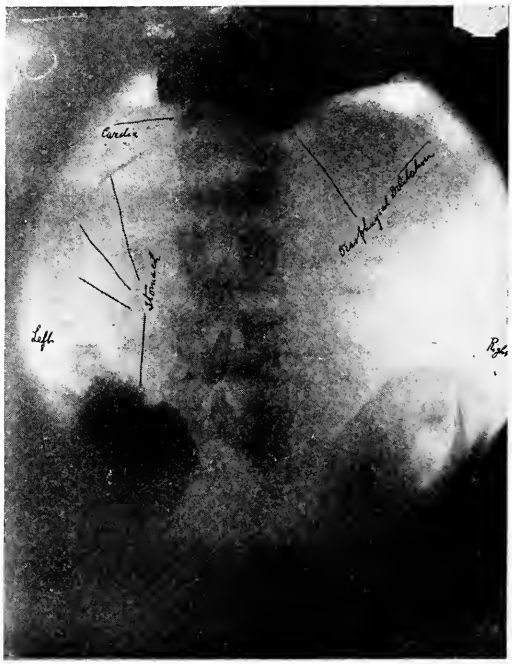
The spread of gastric cancer from its original situation is by way of the lymphatics. Permeating the lymphatics of the gastric wall the malignant epithelial cells reach the subperitoneal group and stimulate the connective tissue reaction in their vicinity with resulting adhesions between the tumor and surrounding viscera, or the abdominal wall. The tumor cells then enter the extragastric lymph spaces and metastasis to glands and distant organs occur. The progress of the epithelial cells through the permeated lymphatics is always followed by a fibrosis of the area involved. Willensky and Thalheimer show that the ulceration in cancer of the stomach is certainly associated with, if not caused by necrosis and the digestive action of the gastric juice. The process is a slow one, and will allow sufficient time for a considerable development of the adhesive and fibrous reaction just described. This barrier thickens as the ulceration approaches the peritoneal coat, and so builds up a resistant wall against the extension of the process. When perforation does occur, the opening is made into a protected cavity and a chronic abscess results. As shown by White, in the case of ulcer such perforations may be revealed by Roentgen ray examination. In our experience chronic perforation of cancer of the stomach indicates an inoperable lesion. Four cases, three acute and one of chronic perforations, have come under our observation.

CASE I.—Acute perforation of carcinoma of the stomach. On August 3, 1908, Mrs. T. S., age 62 years, sought advice for indigestion, which had been annoying her for three months. She had never had indigestion before, and dated her gastric disturbance to an upset following a dietary indiscretion in partaking too freely of sausage. Since then her digestion had been poor, notwithstanding the greatest care in her diet. The patient has lost 20 pounds in flesh and complained of loss of appetite, pressure and abdominal distention, nausea, occasional vomiting and gastric pain, not in any way related to food. The vomited material was light in color, and far in excess of the last meal partaken.

On physical examination the heart and lungs were found normal. The abdomen was much distended and peristaltic waves could easily be made out. A hard mass was readily palpated, which was situated

at about the center of the epigastrium, and which was about 4 c. m. long and 6 c. m. in breadth. The inguinal glands are markedly enlarged. The test meal revealed an absence of free Hcl, presence of lactic acid, and evidence of marked retention. The diagnosis of carcinoma at the pylorus with obstruction was made and operation advised.

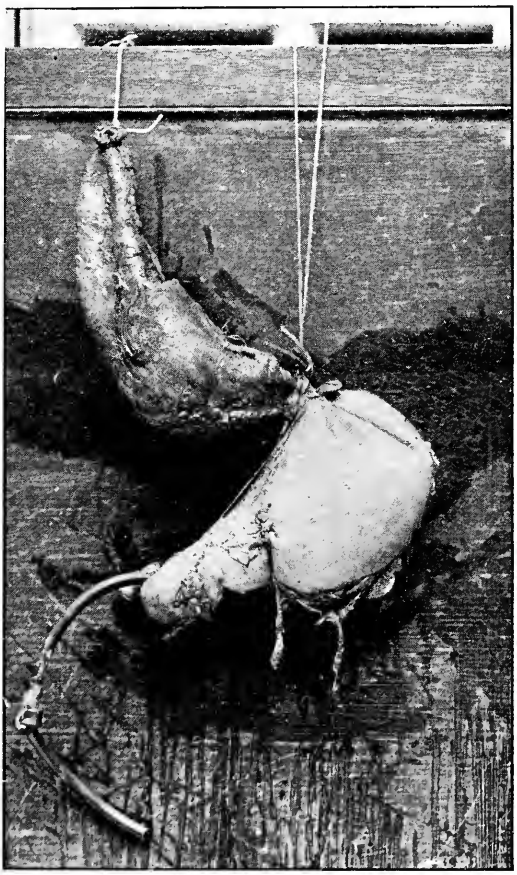
At the operation a large carcinomatous mass was found involving the pylorus and nearly half of the body of the stomach; on account of metastases in the mesenteric glands as well as in the liver, no attempt was made at excision. A gastroenterostomy was performed.



The patient made a satisfactory recovery from the operation, and was able to take nourishment better for a time. The emaciation, however, progressed, and after two months, following operation, the patient became melancholic and developed suicidal tendencies requiring the constant care of a trained attendant. Suddenly on the morning of December 10, 1908, she was overtaken with an intense abdominal pain, which was followed by symptoms of intense shock, a rapid pulse; clammy extremities, cold perspiration; three quarters of a grain of morphia was required within an hour for the relief of the pain; the patient died within a few hours. A partial autopsy was performed, and a large perforation was observed in the midst of the carcinomous

mass at the pylorus. The gastroenterostomy opening was patent, and still functioning normally.

CASE II.—Acute perforation of carcinoma of the stomach. J. S., age 57 years, male, consulted us on January 20, 1910, for a digestive upset, with which he had been troubled for six months. He complained of pain in the region of the stomach, nausea, indigestion, weakness and loss of 36 pounds of flesh.



He was found to be a very emaciated individual with a large mass in his abdomen in the region of the stomach. The gastric contents presented an absence of free Hcl, and contained lactic acid and Oppler Boas bacilli. The diagnosis of carcinoma was made without question. Two days following the examination the patient was suddenly seized with intense abdominal pain, which lasted several hours,

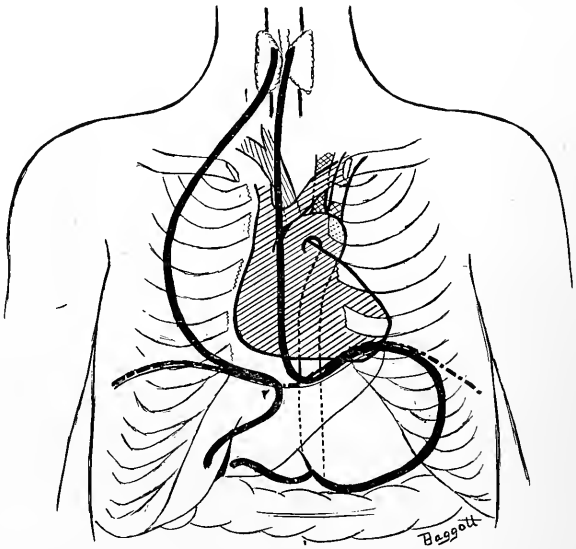
and which was only slightly relieved by hyperdermatic injections of morphia.

The patient died within six hours, and on section an opening sufficiently large to admit a lead pencil was observed in a carcinomatous mass in the body of the stomach. The abdominal cavity was filled with gastric contents.

CASE III.—Chronic perforation, fistulous opening through abdominal wall.

Wm. F., colored, age 53 years, entered the Mercy Hospital on December 6, 1913, and died on December 9, 1913.

The patient has been troubled with indigestion for the past three months; he had nausea and vomiting during this time and suffered from distention and fullness after food. He noted a swelling in the



epigastrium; considerable shortness of breath; loss of strength and flesh. The patient had occasional chills followed by a moderate rise in temperature. There was no history of haematemesis or jaundice; though the stools were frequently tar colored. There was a history of the use of intoxicants and tobacco to excess.

On physical examination the patient is found to be a very feeble and markedly emaciated negro; the heart and lungs are normal. The abdomen is soft and there is a definite mass on the right side just below the costal margin, which is easily palpable, the size of a hen's egg, and which is somewhat nodulated. The inguinal and axillary glands are much enlarged and easily palpable.

Just to the left of the median line and above the umbilicus a scar of an operation is observed situated at the lower angle of the scar is

an ulcerated area in the center of which is found a fistulous opening, connected with the interior of the stomach through a sinus. Milk taken by the mouth discharges upon the external abdominal wall in a curdled state in about an hour after ingestion. The margin of the sinus is stony hard on palpation. A more careful history could not be obtained, nor could a very satisfactory examination be made on account of the great weakness of the patient. A diagnosis of carcinoma with perforation and fistulous sinus was made. The patient died in three days from exhaustion.

At the autopsy a carcinoma of the pylorus was found with metastases in the liver, kidneys and bronchial glands. The sinus extended from the interior of the stomach through the cancerous mass to the external abdominal wall where it opened just above, and slightly to the left of the umbilicus. The fistulous tract consisted of ulcerated carcinomatous tissue and through it the gastric contents were discharged.

CASE IV.—Acute perforation of cancer of the stomach. G. E. W., white, age 73 years, was admitted to the Mercy Hospital, March 29, 1916, on account of severe abdominal pain. The onset of his symptoms occurred at noon, when his trouble was diagnosed acute indigestion. Morphia given at this time did not relieve the pain. Two hours later, he came to the hospital and the great pain, tenderness and rigidity of the abdomen led to an immediate diagnosis of perforative peritonitis. There was no vomiting, but persistent nausea. The general condition of the patient was bad, he was cyanotic, with a rapid pulse and showing every sign of great distress. There was dullness in both flanks. A ruptured cancer of the stomach was considered the cause of the peritonitis, because of the history of a six months period of indigestion and a loss of 25 pounds in weight during this period. Operation was advised and accepted.

Operation March 29, 1916, 3 p. m. Anesthesia novocaine and ether; right rectus incision with transverse cut at upper angle; gelatinous fluid in peritoneal cavity. The perforation, about 1/16-inch in diameter, was found in a small annular cancer near the pylorus. Apparently the omentum had been loosely adherent to the opening. The opening was burned with the cautery and the area turned in with mattrass sutures. The omentum was sutured over this region. Drains were carried to the region of the perforation and the right kidney fossa. The pelvis was drained through a suprapubic wound. The patient rallied from the anesthesia, but died about 36 hours after the operation. A post-mortem examination was not permitted.

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[1] Riegel's Diseases of the Stomach (edited by Stockton), 1903, p. 698.

[2] Perry & Shaw (Guy's Hospital Report, 1904).

[3] Smithies (Cancer of the Stomach, 1916, p. 101).

[4] Friedenwald (A Clinical Study of One Thousand Cases of Cancer of the Stomach), *American Journal of the Medical Sciences*, November, 1914.

THE X-RAY TEST OF GASTRIC MOTILITY.

By Dr. R. Walter Mills,

st. louis.

The final value of a clinical test does not lie alone in the proportion of cases of well-marked disease which it will indicate, but also in the additional percentage of slight and early cases which it can be made to detect by taking into consideration influencing factors. With experience the lesser reactions of many clinical tests often become valuable because indicating beginning, slight, less readily recognizable and more frequently controllable disease.

It is obvious that the X-ray gives a true expression of gastric motility in the case of the individual under examination on the specific occasion of observation with the test substance employed. The contradictory experience of different workers with the X-ray motility test is due not to the inaccuracy of the method but to lack of knowledge of variation in the time of total gastric motility in different persons and under different conditions and to lack of a standard technique.

To successfully utilize the X-ray as a motility test we must have a clear idea of those factors that influence gastric motility.

The present paper represents an effort to add to our knowledge of and classify factors influencing gastric motility; the effect of disease both organic and functional, primarily gastric and not primarily gastric, the influence of habitus and of general conditions.

Comparative findings are based on 1,000 successive studies in all of which cases the time of gastric emptying was determined to within 15 minutes unless a residue was present at six hours in which instance observations were discontinued.

A second series of 1,000 subjects without organic or marked functional disturbances has been compiled to show comparative motilities in different types of individuals.

Data from consecutive graphic studies of 2,500 patients has been tabulated to show the constancy of relationship between gastric form and position and bodily type, this to test the pro-

priety of utilizing bodily habitus as a basis for judging gastric motilty. A sub-table of 1,000 cases of these has been arranged on the basis of freedom from frankly abnormal conditions.

In every case cited pyloric tonicity has been studied, observations being standardized by dividing the time after both the preliminary water mixture and the later fermillac mixture into three periods, noting the degree of active initial motility in the first period, and of active and passive pyloric canalization in the second and third periods by a standardized abdominal manipulation in terms of certain degrees. Similar observations were made during the later stages of motility.

The test meal used was a standard and average contrast meal. The results of observations have been arranged in tabulations of groups also arranged on a basis of bodily habitus in order to test the influence of such on the time of gastric motility. Subjects studied are from both hospital and private sources. I wish to express my appreciation of the encouragement offered by my associate, Dr. Soper, and the heads of the Departments of Medicine, Surgery and Roentgenology at the Barnes Hospital.

Conclusions are based on X-ray observations after a standard contrast test meal. That the same condition obtained after ordinary meals of like physiological demand is highly probable.

The X-ray method of studying gastric motility is valuable because allowing observations of its rate total time, mechanism and impairments. The X-ray affords a most delicate test of gastric motility, in fact in this lies its weakness as well as its strength, for it is so delicate a test that it is difficult to interpret its lesser variations.

It is not possible to devise an X-ray time test probably any sort of motility test, that will indicate slight degrees of motor insufficiency due to disease in certain cases that will not give a like result in other subjects where such must be considered normal or functional on account of variation in the time of motility in different types of individuals and of the influence of physical and nervous conditions. On the other hand, a stomach may empty just within our arbitrary six-hour period, yet such time be slow for that particular individual as judged by others of like type and condition. The six-hour period after the usual X-ray test meal should be regarded as a standard of comparison. A residue at such time does not invariably indicate organic or functional

disease or necessarily an abnormality, though the impression grows that it never occurs under admirable conditions. By taking into consideration influencing factors the test becomes a powerful aid to clinical diagnosis.

Bodily habitus is the most constantly influencing factor through the associated degree of tonus the resulting stomach form and possibly through the degree of peristalsis in determining the time of gastric total motility which time is most effectively judged on a basis of physical type.

A relationship between the time of total gastric motility and the type of individual rather than the type of stomach is fundamental. Many anatomical and physiological variations as in the degree of tonus the form and motility period of the stomach are apparent. There are common relationships between them, but they are not basic and the same orderliness cannot be obtained by attempting a classification on such foundation as is the case where habitus is considered fundamental.

The degree of tonus of the stomach is the chief direct cause in determining the time of its total motility, this through the degree of intra-gastric pressure resulting, the form of the stomach and the consequent influence of gravity. Where the stomach is disharmonically hypertonic gastric total motility is commensurably rapid. Less markedly where tonus is similarly poor motility tends to be corespondingly slow. A series of cases of gastric hypotonicity and ptosis judged on a type basis show 28 per cent. of hypomotilities. In cases of increased intra-abdominal tension as from tumors and ascites gastric motility is always prompt, usually overprompt even when patients are very ill. The tonus of the pylorus in adults, whether spastic or lax, seems of slight effect in determining the time of total gastric motility except in cases of organic peripyloric stenosis and even here the motor delay is directly proportional to the degree of stenosis and not to the "pylorospasm." Cases in which the initial tonicity of the pylorus was so marked as to cause their classification as instances of pylorospasm showed slightly slower total motility than the average—21 per cent. of six-hour residues—possibly within the bounds of variation, as the series was not large. A group of cases in which the uninvolved pylorus was strikingly incompetent showed 8 per cent. of delayed motilities, suggesting that the condition has certainly no great influence on the time of total motility.

Gastric hypomotility, of which every conceivable variation occurs, is of great clinical interest as the recognized cause of the symptoms of certain conditions and probably of many others not as yet recognized. Gastric hypermotility has no clinical interests except in certain gross pathological conditions associated with an elevated contracted stomach and incompetent pylorus such as occurs in scirrhus carcinoma and in cases having over-prompt gastro-enterostomy stomata.

Three types of delayed gastric motility associated with organic lesions may be recognized as to the manner of their causation. First, frank peripyloric stenosis in the great majority of instances of duodenal ulcer origin. Second, crippling of the expulsive mechanism of the stomach as the result of either benign or malignant involvement. Third, secondary inhibition of gastric motility apparently due to decrease or abnormality in peristalsis and characteristically associated with a lax pylorus, such may be of either gastric or extra-gastric causation. Examples are restricted ulcer of the upper portions of the stomach and gall-bladder disease. Different motility impairing factors often act complexly in different degrees in the same case. The striking delay in motility in cases of restricted gastric ulcer of the upper stomach associated with a lax pylorus suggests a break in the path of conductivity of impulses governing peristalsis and further an analogy with certain cardiac conditions.

The cause of the symptoms of frank peripyloric stenosis are recognized, but it is of great interest that certain of the gastric symptoms associated with the other conditions and commonly considered reflex are very possibly due to gastric hypomotility demonstrable by the X-ray.

Eighty-nine per cent. of gastric ulcers showed delayed gastric motility. The delay is chiefly of the inhibitory, less frequently of the crippled mechanism type and rarely due to prepyloric stenosis still more rarely associated with demonstrable pylorospasm.

Forty-eight per cent. of duodenal ulcers were associated with delayed motility of every degree, due to mechanical narrowing about the pylorus and possibly contributed to in some cases by pylorospasm.

Ninety-one per cent. of cases of gastric new growths showed delayed motility in the great majority of cases due to crippling

of the musculature of the stomach, a reflection of the value of the food retention findings of clinical methods.

In achylia gastrica motility is slightly more rapid than the average. The tonus and action of the pylorus show no difference from that noted in non-achylous cases.

Gastric hypomotility occurs reflexly in certain general conditions of a functional nature, but should only be accepted as a result of such if it can be demonstrated, by a considerable number of cases, that the association is constant and no other influencing factors are present. Examples of such depressive conditions are attacks of migraine in which 64 per cent. of the cases show hypomotility and less strikingly general debility and certain marked neurasthenic conditions. Gall-bladder disease shows a most interesting suggestion of gastric hypomotility, 32 per cent. of the cases having six-hour residues. It is of interest in this connection that cases of appendicitis are associated with but 15 per cent. of hypomotilities, within the bounds of normal variation.

	1.	Habitus diagrams.
Habitus....	2.	Type (habitus) motilities. Hypersthenic.
	3.	Type (habitus) motilities. Sthenic.
	4.	Type (habitus) motilities. Hyposthenic.
	5.	Type (habitus) motilities. Asthenic.
	6.	Total motility times. Different types.
	7.	Correspondence of stomach to habitus. Tables.
Groups Organic....	8.	Group 1. Duodenal ulcer.
	9.	Group 2. Gastric ulcer.
	10.	Group 3. New growths.
Groups Functional.	11.	Group 5. Gall bladder.
	12.	Group 6. Appendicitis.
	13.	Group 7. Hypotonicity and ptosis.
	14.	Group 8. Hypertonicity.
	15.	Group 9. Intra-abdominal tension.
	16.	Group 10. Headache.
	17.	Group 11. Achylia.
	18.	Group 12. Pylorospasm.
	19.	Group 13. Incompetent pylorus.
	20.	Group 14. Miscellaneous factors.
	21.	Group 16. Unknown factors.

22. *Group* 17. *Summary organic and functional factors.*
23. Group 18. Summary six-hour residues. Organic function unknown.
24. Plate. Last contents passing through pylorus.

EXTRA PLATES.....

25. Scirrhus carcinoma (Mrs. Keelor).
26. Prepyloric ulcer (Gruya).
27. Gastric lues (Schulte).
28. Gastric ulcer (Catron).
29. Gastric ulcer 24 hours (Catron).
30. Gastric ulcer, open pylorus, crater.
31. Gastric ulcer, duodenum full crater (Mrs. W. Reinhardt).
32. Migraine, vomiting.
33. Migraine, vomiting, open pylorus.
34. Ca. stomach, open pylorus (Sommer).
35. Duodenal ulcer "pylorospasm" (Kuntz).

DR. R. WALTER MILLS (Demonstrating slides after reading paper): The first table shows the method of tabulating results and establishing a line of average motility in studies of gastric total motility. The subjects in each table are grouped according to their physical type and the total motility period is shown in hours and quarter hours. No effort has been made to record the total motility time any more exactly than that such occurred within a certain fifteen minute period.

The first table shows the time of average motility in subjects of the great or hypersthenic habitus. As will be seen the average emptying time is 4 hours and 15 minutes.

The next slide shows the time of average total motility in subjects of sthenic habitus, 4 hours and 45 minutes. It will be seen that the average line is further to the right in each succeeding table as the habitus becomes less sthenic and more asthenic. In other words, the periods of gastric motility in different habiti form a gradient paralleling variations in physical types.

This table shows the average motility in individuals classed as hyposthenic, such time being 5 hours and 30 minutes.

The following slide shows the motility time in asthenics 5 hours and 45 minutes. It will be noted in this type that a considerable

number of these asthenics have a gastric motility not complete within six hours.

The following slide shows tabulations of two groups of cases arranged on a basis of bodily habitus to show the constancy of relationship of stomach form and position to bodily type. This to demonstrate the propriety of judging gastric motility on a basis of bodily habitus rather than stomach form or tonus, these being but attributes of the former. The first group contains 1,000 cases; the second group 2,500. The tables indicate much of interest aside from the point in question. For instance, as to the incidence of habitus as related to sex. It will be noted in general that dominantly sthenic characteristics are progressively less common in women as they become marked, and asthenic peculiarities less common in men. It will be noted that the stomach corresponds to the habitus approximately 75 per cent. of the cases, judging such relationship on very close standards which amount practically to anticipating in advance exactly what type of stomach will be found in a certain individual; conclusions indicate that this can be done in 75 per cent. of all cases. The second series of 2,500 subjects contains pathological cases which, of course, greatly reduce this percentage.

The following slides show the incidence of gastric hypomotility in certain organic conditions, such hypomotility being judged by six-hour residue.

The first is a series of gastric ulcers. It will be noted that 88 per cent. showed hypomotility. A very interesting thing with regard to delayed motility and gastric ulcer is that pylorospasm is not a usual factor in causing such, as has been mentioned. This slide shows the percentage of delayed motility in duodenal ulcer, approximately 60 per cent. of the cases. As an aside, these last two tables show an interesting point as to the incidence of gastric and duodenal ulcer in our work, that is approximately ten duodenals to one gastric in private patients and one to three in clinic cases, suggesting that gastric ulcer is more common among the poor or else gastric ulcer being a most severe disease we see a larger proportion of them among clinic patients. The figures of the Mayo clinic were thought to strikingly show the predominance of duodenal ulcer, but the proportion of duodenal to gastric ulcer in this series is much greater than in theirs. I believe that the cause is that a great many cases of duodenal

ulcer are so mild that a smaller proportion of them make the journey. Probably a great many people with duodenal ulcer never see a doctor.

The next group shows a series of gastric new growths of which approximately 87 per cent. showed delayed motility.

In this slide are shown gastric motilities in gall-bladder diseases. A very interesting thing is that there are 33 per cent. of these showing hypomotility suggesting a definite influence of such condition on stomach motility, possibly accounting for certain of the dyspeptic symptoms in gall-bladder disease.

In this table are arranged cases of gastric hypotonicity. The results suggest that lack of gastric tonus per se has much less effect in delaying motility than we had supposed.

Here we see cases of intra-abdominal tension as from tumors, ascites, etc., and most strikingly no case shows delayed gastric motility, though some of these patients were almost moribund at the time of examination.

Cases of migraine as shown in this slide indicate a quite constant delay in motility suggesting that such may be a factor in certain of the symptoms of sick headache. Delayed gastric motility is here not due to pylorospasm, as the pylorus in all cases was demonstrated as unusually patulous and incompetent.

The present slide shows the time of gastric motility in achylia gastrica. You all know of the general opinion of a hypermotility in this condition after ordinary test meals. Curiously after the X-ray test there is a slight, but only a very slight, suggestion of increased motility. Interestingly, too, there was no difference in the contractural activity of the pylorus in these cases that differed from cases where normal acidities were present, suggesting that there must be other factors than the accepted pyloric acid reflex in controlling gastric motility in achylia.

In this group we see a tabulation of cases in which there was what I have classified as initial pylorospasm; that is, no canalization of the pylorus occurred either passively or actively as a result of palpation for one-half hour after the ingestion of the contrast meal. In spite of this initial pylorospasm these cases show but a very slight delay if any in the time of total gastric motility.

Another group showing cases associated with incompetent pylorus. It will be noted that this condition apparently in no way influenced the time of total gastric motility, especially that

such was not more rapid than the average for the different types of subjects.

DISCUSSIONS.

DR. LICHTY: This interesting and well presented subject is before you now for discussion.

DR. JACOB KAUFMANN, New York City: I think that Dr. Mills is quite right when he says that the value of his tabulation is the fact that it is based on the differentiation of types. It seems to me that modern studies of constitutional and developmental factors will give us a better understanding of the shortcomings of these different types. These types which show marked differences in growth are often the result of abnormalities in internal-secretion activity, either during prenatal life or arising after birth through the obnoxious influence of infectious diseases. The well known deleterious effect of the diphtheria-toxin on the adrenals, for instance, when it appears early in life, may have a marked influence on the development of the chromoffin system and the body in general.

The reaction of individuals of different types will differ, as I shall have occasion to point out in my paper. Dr. Mills mentioned the great frequency of pronounced gastric insufficiency in patients of the asthenic type, who suffer from migraine. In corroborating the frequent experience of pronounced gastric atony of the stomach in combination with migraine.

DR. KAUFMANN: I wish to emphasize that both disturbances, the headache and the gastric atony, are the result of a general disturbance, a general asthenia and not, as so often is erroneously stated, the one a result of the other. A general tabulation of motor disturbances of the stomach on a basis of types will greatly promote an understanding of the subject.

DR. JOHN C. HEMMETER, Baltimore, Md.: Gentlemen. It is a good sign that this meeting starts with such a scholarly paper, that gives evidence of such great interest in this subject. I only regret that a paper containing such a wealth of information should have to be presented in fifteen minutes. Dr. Mills has brought before us a long series of personal studies, and, I dare say, if he had twice as long a time, he could bring home his deductions better to us.

I desire to emphasize the fact that Dr. Mills has studied his cases from the perspective of what he prefers to call the *habitus;* and that is, a condition for which the individual is not blameable. The word *habitus* was first used by Stiller. It is a state of constitution with which the individual was born. Some fifteen years ago (?) I read a paper on the anthropometric measurements in this condition, and called attention to the fact that if you lay a pair of compasses on the xiphoid cartilage and place the bars along the end of the short ribs, this would give an angle which I called the *sub xiphoid angle,* which is an exponent of the personal habitus.

It looks as if we were breeding a human race with displaced viscera, splanchnoptosis is on the increase, and these conditions are inherited and not altogether blameable to errors of diet or diseases during life, but were brought into existence with the birth of the individual.

It might be conceivable that they pre-existed in the parents and grandparents of the individual for I have been able to trace the heredity factor in at least four families back to the third generation presenting the present youngest individual suffering from *splanchnoptosis*. The patient in one family is 16 years old and has a floating kidney and coloptosis and gastroptosis. The father is 38 years old, has splanchnoptosis. The grandfather is 61 years old and has the same abnormality and he states that his mother died with complications due to floating kidney.

DR. MAX EINHORN, New York City: I should like to speak of only one point in regard to the paper of Dr. Mills, and that is achylia gastrica. I am glad that he found that the pylorus is not open in achylia, as some believe it to be. I found, years ago, that in achylia gastrica the gastric contents are usually very thick, and that the water is not to be found in the stomach contents as it is in normal individuals, for instance, an hour after a test meal. I ascribed this to the fact that there was less fluid in the stomach with achylia, because there is no secretion going on in that condition. The fluid leaves the stomach more quickly than other portions of the diet in any case, and in achylia there is no addition to the fluid that is imbibed caused by secretion. Hence, after a while, we find only solid particles in the viscus. It appears as if the stomach empties itself more quickly in that condition, but this is only an appearance. In reality, it empties itself just as in ordinary cases, and I am glad that, according to the findings of Dr. Mills, this seemed to be the case.

DR. MILLS, closing: I wish to thank the members much for their kind criticism. I am sorry that Dr. Levy is not with us on account of illness in his family, as I had looked forward to an interesting discussion of the stomach tube versus the X-ray as a means of studying gastric motility.

It was with some questioning that I presented the results of gastric motility as observed by the X-ray in cases of achylia, this because the results seemed so at variance with accepted teachings. However, these results are facts and as such can not be denied. Dr. Smithies spoke of the X-ray test meal as being an alkaline meal and as objectionable on this account. The barium fermillac meal is not an alkaline test meal but gives a distinctly acid reaction and moreover is essentially a protein meal exciting acid secretion. In some experiments made in connection with Dr. Gorham of St. Louis, gastric acidities after the usual barium fermillac meal were found approximately those that occurred after the standard Boas-Ewald meal. I cannot accept the idea that the X-ray test is not an adequate test of gastric motility. One cannot prove that motility is the same as

in instances where the same test meal is used without barium, but the probability is that results are approximately the same. The barium is inert and nothing but an indicator. The fact that impairments of gastric motility in different disease conditions do parallel clinical findings, which is the gist of my paper, suggests the accuracy of the test. We have used the X-ray method in conjunction with the ordinary clinical retention test and the results parallel each other consistently; in fact, there is reason to believe that the X-ray is the more delicate test. I do not doubt that the tube may *some times* show abnormal motor conditions that the X-ray method does not, but such results are not common. The fact that eminent physiologists have had no hesitancy in using the ordinary X-ray contrast substances in tests of motility is worth recalling.

I did not have the opportunity of emphasizing a fact that I should like to mention now, namely that in disease conditions in which the gastric wall is intact yet impairments of motility occur there is a constant reflection of the influence of habitus on the time of such impaired motility. For instance, in duodenal ulcer occurring in robust sthenics a smaller percentage show delayed motility than in similar cases occurring in asthenics. The slower normal motility of the asthenic makes for a larger percentage of six hour residues than occurs in the sthenic.

Dr. Frank Smithies, Chicago, Ill.: I was a bit discouraged about this question until I saw that Dr. Mills had shown that a large portion of the cases have physical departures from the "so-called" normal that have existed from birth, and are yet not incompatible with longevity or moderate comfort. The point that Dr. Mills has made is that he has established from a large series of cases a standard for the roentgenologist of what will happen when bariumized or bismuthized food is given by mouth and passes through stomach and bowels and has established this standard in relation to certain so-called normal or pathological physical imperfections. This is an important service, yet no one can say that the stomach will act in the same way in the presence of an X-ray motor meal as in the presence of a normal food, which excites certain normal physiologic stimuli. He has also established what will happen when the stomach works under more or less constant alkalinity. This is what happens when one gives such a large mass of barium or bismuth as a test motor meal. But he has not established what will happen in an individual who lives on real food. This has been previously emphasized, first from the older studies of many men in this organization and later from the fractional method of Rehfuss. The discrepancy between the gastric motor factor by the X-ray method and when real food is given is shown by certain observations made by me long since. In benign peptic ulcer there was eight hour or more residuce in less than forty-one per cent. Yet figures here presented show over eighty per cent. of rsidue by the X-ray method. In duodenal ulcer, the essayist noted

over sixty per cent. with residue by the roentgen method; yet, using real food we had an eight hour residue in rather more than forty-five per cent. Figures in gastric cancer are similar—more than ninety per cent. by roentgen observation and in 92 cases using unaltered food we had retention in about 74 per cent. Hence Dr. Mills has established a most interesting retention meal standard for the X-ray observer. It will doubtless be found that his figures correspond closely to those of other X-ray men. But this standard has little bearing with regard to what happens when normal food is placed in the stomach and then is permitted to excite normal secretory and motor mechanism, both of which, the observations of Palow, Cannon and Carson have shown are closely allied and are interdependent.

THE OPAQUE MEAL VERSUS THE STOMACH TUBE IN THE DIAGNOSIS OF GASTRIC HYPOMOTILITY.

By I. H. Levy, M. D.,

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It is generally conceded that the motor function of the stomach is of greater importance than either its digestive or absorptive. Anything interfering with its normal emptying, interferes with the general process of digestion. Hypomotility, as I use the term, does not refer to a lowered muscle tone; but a failure of the stomach, whatever the cause may be, to get a meal into the intestine within a definite time, known as normal. It is well known that stomachs differ in size and rapidity of digestion, and that a number of factors like kind of food, size of meal, position, mental state, etc., modify the evacuation time. However, delay beyond a certain period becomes pathological. There is, as yet, no uniformly accepted procedure for determining the gastric emptying time. It is, however, common practice to consider food found in the stomach in the morning after a hearty evening meal as indicative of a severe grade of motor insufficiency. Food found in the stomach seven hours after an ordinary meal is diagnostic of the milder grades.

The Roentgen-ray diagnosis is based on a residue six hours after the ingestion of an opaque meal. Unfortunately, however, no standard technique has been followed by roentgenologists. The kind and quantity of opaque salt used differs. Some use a liquid vehicle like buttermilk or cocoa, others a more solid one like bread and milk, or cereal. The amount of opaque salt varies from two to six ounces; the total amount of the meal, from six to twenty. There is even no uniformity of practice in regard to eating between the first and six-hour observation; nor is the stomach always emptied previous to beginning the examination. Conclusions drawn from such diverse procedures should not be contrasted. The technique of the opaque meal should be standardized, like the Boas test-breakfast.

Two years ago I reported, with Dr. Kantor,[1] 185 cases of delayed gastric emptying occurring in an unselected series of

1,600 patients with digestive symptoms. I am now able to report 1,000 additional cases studied both with the tube and the Roentgen rays.

Technique.—After a complete history and physical examination, the patient presents himself in the morning fasting. The tube is introduced and the contents aspirated. The Ewald test-breakfast is then administered and extracted one hour later. Occasionally the Rehfuss fractional method is employed. The Roentgen examination follows. The meal consists of 100 gm. of barium sulphate in 500 c.c. of buttermilk. The usual fluoroscopic and radiographic examination is made, and the patient instructed to return in six hours and warned not to eat or drink in the interval. On the following day he is requested to eat a regular meal consisting of meat, potato, bread and some light dessert; the quantity to correspond with what he usually consumes at dinner, and to present himself seven hours later not eating or drinking in the interval. The object of the visit is not disclosed, so as to eliminate the psychic factor. The tube is then introduced, the contents aspirated, and the stomach washed out. As the stomach should be empty at this time, the amount of residue determines the degree of motor disturbance.

Analysis of the 1,000 cases showed hypomotility with the opaque meal 100 times, with the tube 141. In no single instance did I fail to find some food in the stomach with the tube when any of the opaque meal was visible six hours after. Occasionally the tube rest was less than the opaque meal rest indicated. On the other hand, in 41 cases the tube gave evidence of delayed emptying when the Roentgen method failed to discover any residue. As a rule these cases are of the milder forms of motor disturbance. However, there were 9 cases in this group with a typical duodenal ulcer history. Two of these were verified at operation. There was one case of gastric ulcer, also proved at operation. There were 8 cases of chronic appendicitis. Four of these were operated and the diagnosis verified. I believe that chronic appendicitis is very frequently associated with a mild form of hypomotility sufficient to give a moderate seven-hour rest with a Riegel meal, but none with the six-hour opaque. But, besides these 41 cases, there were 22 others that gave but a minimum six-hour X-ray rest in which the tube showed a large rest; in one case, as much as 800 c.c.; in a number of others,

over 150 c.c. From the above study, I would conclude that the seven-hour tube test is superior to the six-hour opaque meal method as practiced by roentgenologists in the diagnosis of gastric hypomotility; for in 28 per cent. of the cases it gave evidence of a rest not discovered by the Roentgen method, and in 17 per cent. more it showed a marked hypomotility where the Roentgen method indicated but a slight disturbance. In both groups there were a number of surgical conditions.

I am aware that these conclusions are not in accord with those of Carman and Miller[2] of the Mayo Clinic. They state that "During the year 1914, 950 patients who had been examined both by the Roentgen ray and the test-meal went to operation. Two hundred and twenty of these, or 23.1 per cent., showed a gastric residue, at the Roentgen-ray examination, from the six-hour meal. One hundred and thirty-one, or 13.7 per cent., had food remnants. In other words, the Roentgen ray showed approximately 70 per cent. more retentions than did the clinical test-meal." In attempting to explain the discrepancy between the tube and Roentgen findings, Carman and Miller say: "It would seem probable that the time elapsing between the ingestion of the gastro-enterologist's meal and its withdrawal is too liberal, and pathologic hypomotility existed." I believe that this explanation hits the nail on the head. It is hardly just to compare a six-hour opaque meal residue with a 14-16-hour tube one. A stomach may suffer from a decided degree of hypomotility and yet manage to empty itself during the night. The six-hour opaque meal and the "fasting contents" rest may be sufficient to detect gross surgical lesions, but they are not delicate enough for all clinical purposes. For the clinician, even in the non-surgical conditions it is important to recognize these cases of hypomotility, as they give rise to definite symptoms. The stomach should be empty of one meal before the next is introduced. The healthy stomach is capable of a great deal of abuse. It can tolerate a second meal on top of the previous one. However, the digestive juices at the end of a meal are not quite the same as at the beginning. In a stagnating stomach, six or seven hours after a meal, the contents are decidedly abnormal. There may be fermentation; the odor is frequently foul and rancid, and abnormal products of digestion formed. Pouring fresh food into such a stomach at once leads to the souring of the fresh meal.

These patients suffer from fullness, belching and a variety of toxic symptoms. They believe the food eaten at the last meal responsible for their distress. It is not the last meal, but the remains of the previous one that produce the symptoms.

Harmer and Dodd[3] call attention to the difficulty of always emptying the stomach with the ordinary tube; but, despite their contention, it is my opinion that, with a properly constructed tube, a proper technique, and a bulb extractor, the stomach can with very rare exceptions be emptied of its contents.

It might be suggested that the Roentgen method could be made more delicate by shortening the emptying time from six to four hours, or even less. Or the Roentgen method might be combined with the Riegel method as suggested by Cole.[4] He says: "In a previous communication[5] I have already shown the fallacy of testing the gastric motor efficiency by administering bismuth suspended in fluid or mixed with cereal, and the same is true for intestinal motor efficiency. If the test is to be of value the stomach and intestines must be called upon to evacuate such a meal as is normally imposed upon them. Therefore the true test of gastro-intestinal motor efficiency is made by administering bismuth or barium, suspended in fluid, preferably buttermilk, *in conjunction with* a Riegel meal of meat, potatoes, and bread."

To shorten the Roentgen method, I believe, would be unwise, as roentgenologists, as a rule, are rather more particularly interested in the discovery of actual lesions than functional disturbances. Too much surgery is now being done on misinterpreted Roentgen evidence, and to shorten the time would increase the evil. I am in accord with Bassler,[6] who states: "It is apparent, whatever has been advanced to the contrary, that the method of examination by food extraction is decidedly more to be depended on in gaining an idea of exit from the stomach than is the bismuth Roentgen-ray method." But the most serious objection to the opaque meal as a test for hypomotility is that these salts do not enter into the human dietary. For practical purposes it matters very little how long these substances remain in the stomach. It would seem more rational to test its motor function by giving the patient a meal he is in the habit of eating. If the Roentgen method simply determined the length of time that an opaque meal remained in the stomach, its use could entirely be dispensed with. This could be determined just as

well with the tube, and the patient spared the expense and the physician the danger of X-ray exposures. To accomplish this, it would only be necessary to substitute the Rieder meal for the Riegel. The opaque meal could be administered as for Roentgen work. The tube could be introduced six hours later and the amount of opaque salts remaining could actually be measured and weighed; or, better yet, the fractional extraction method of Rehfuss could be used and the exact time that the bismuth remained in the stomach determined.[7]

But the tube tells us more than that a rest is present. From the character of the residue we learn whether the patient masticates his food thoroughly; just what food is difficult for him to expel; whether abnormal products of digestion are present; whether fermentation is taking place and whether there is hemorrhage—all this information is easily obtained and is valuable in diagnosis and treatment.

It is not my intention to belittle in any way the importance of the Roentgen diagnosis of gastro-intestinal conditions, nor do I advocate disregarding the Roentgen evidence in hypomotility. It is simply my purpose to emphasize that a rational test for gastric emptying should be based on a meal of ordinary bulk and complexity, which the patient should dispose of in seven hours, and that the Roentgen-ray test as commonly practiced is not sufficiently delicate for many clinical purposes.

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MASSIVE HEMORRHAGE FROM THE GASTRO-INTESTINAL TRACT, ASSOCIATED WITH ARTERIAL DISEASE AND HYPERTENSION.

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Introductory.

Within a period of scarcely more than a year, I have had occasion to observe the occurrence of massive hemorrhage into the digestive tract in three patients, as a result, apparently, in each instance, of a diseased state of the arterial system with an especial localization in the vessels of the stomach and duodenum.

While this assumption could not be verified, because of a lack of opportunity for making direct inspection at the site of the hemorrhage, nevertheless the close association exhibited by the vascular accident in each case, with a manifestly morbid state of the arterial system as a whole, has seemed sufficient to justify the establishing of some definite relationship between the two conditions.

Notwithstanding the fact that rupture of an arterial vessel, weakened by arterio-sclerotic degeneration is an event of relative frequency in many other organs, from a careful survey of the literature, it would seem that a similar accident along the gastro-intestinal tract is one rarely to be expected.

That the possibility of this condition does exist, however, and that it may become at times a source of profuse gastro-intestinal hemorrhage has been demonstrated to me with sufficient emphasis in the following three cases.

Report of Cases.

Case I.—Rosa N., age 68, mother of nine children, seven living. Past History.—Had the various infectious diseases of childhood in mild form. At the age of 22, a moderately severe attack of typhoid fever. During the yellow fever epidemic in the South in 1867, the patient claims to have had a severe form of the disease. After her 30th year

she had several attacks of acute, articular rheumatism, the last of which occurred eight years ago.

The menopause took place during her 48th year and was accompanied by many of the usual nervous phenomena. While up to this time there had been no history of dyspeptic trouble, now a tendency to gaseous distention of the bowels was noted, occasioning much distress at intervals, mainly in the form of sticking pains in the left upper abdomen. The bowel evacautions have always remained free and regular.

In 1904, during the patient's 54th year, the first attack of hemorrhage into the gastro-intestinal tract occurred. The day preceding the attack there had been some slight digestive disturbance, for which the attending physician had prescribed a calomel purge. During the early morning hours of the following day, the patient was awakened with a feeling of intense nausea and faintness, and shortly after vomited large quantities of dark, clotted blood. There was extreme languor and other evidences of shock incidental to a large hemorrhage. In the afternoon of the same day a recurrence of the blood vomiting took place, even more copious than before, with the evacuation simultaneously of dark red and tarry feces. A tentative diagnosis of latent peptic ulcer was made at the time by the physician in attendance, as an explanation of the hemorrhage. A detailed plan of medical treatment for peptic ulcer was followed, covering a period of six weeks, resulting in apparently complete recovery. At this period the patient had been living in a small Alabama city, but in 1908 she moved her residence to New Orleans, when she first came under my observation.

No further evidence of disturbance of the digestive organs had taken place at this time, but for a year previous she had noticed blood in the urine at intervals, which had given rise to some anxiety. Examinations of the urine made by me in 1908 showed, besides the presence of small quantities of blood, occasional hyaline and granular casts. There was a moderate hypertrophy of the left heart present and the blood vessels were found to be thickened but were not calcareous. The systolic blood pressure at this time was 180.

A mild hematuria has persisted intermittently up to the present day. No further evidence of genito-urinary disease has developed, however, other than a progressive chronic nephritis. Cystoscopic examination has been refused by the patient persistently, but in the opinion of my urologist confrere, Dr. Nelken, the urinary hemorrhage is the result of the slow seepage of blood into a nephritic kidney under the influence of a constantly raised arterial tension.

In January, 1917, without any prodromal symptoms, a second hemorrhage into the digestive tract occurred. According to the patient's statement, the amount of blood vomited on this occasion was not quite as large as in the previous attack. However, from personal observation, the quantity of the vomitus reached fully a pint and a half and the stools remained tarry for fully five days.

Immediately prior to the attack, the blood pressure had been noted

at 240 systolic and 115 diastolic. As a result of the copious blood letting, there was a prompt fall in the systolic pressure to 150.

In spite of the profuse nature of the hemorrhage, the patient made comparatively rapid recovery and within six weeks the blood picture returned to the normal. Concurrently, however, there appeared a tendency to progressive ascendency in the arterial tension which has since remained constantly around the 200 systolic and 110 diastolic point. Repeated examinations have subsequently failed to show the presence of an occult blood reaction in the stools.

Status Presens.—The patient is of obese type, with small stature and florid complexion. The surface arteries are hard and moderately nodulated. The pulse is full and bounding with regular rhythm.

The heart is enlarged to the left, past the mammary line. A soft systolic blow can be heard at the apex, transmitted to the left. At the aortic area, the sounds are distinctly roughened, and the aortic closure is loud and sharp.

The abdomen is soft and allows of easy palpation. Neither the liver nor the splenic edges can be felt. No areas of tenderness have been noted at any time.

The blood examinations reveal nothing abnormal. Wassermann reactions are negative. The urine is of a constant low specific gravity and contains occasional casts. Blood cells are frequently present, as described above.

The general health of the patient has remained good in the interim since recovery from the last hemorrhagic outburst.

Epicrisis.—In the history and course of this case, the arterial factor would seem to play a most important role. There is unmistakable evidence of a general arterio-sclerosis present, and the persistent hemorrhage into the genito-urinary tract is in itself apparently of purely arterial origin. The two attacks of massive gastric hemorrhage, appearing without previous digestive disturbance, are likewise suggestive of a direct arterial origin. In the absence of any other cause, it is reasonable to assume that the diseased state of the arterial system must bear some etiological relationship to the hemorrhage, either by inducing the formation of a peptic ulceration, or else by inviting direct rupture of a diseased vessel wall previously weakened by degenerative changes.

CASE II.—J. T. N., male, age 42, married, insurance solicitor by occupation.

Past History.—Had yellow fever at the age of 2 years. In 1898, had one attack of malarial fever of the intermittent type, which he claims lasted three months. Five years ago, he had a severe form of measles. Venereal infection is denied in toto and the patient has never been addicted to the use of alcohol or tobacco.

Shortly following the attack of malarial fever, a tendency to repeated and mild gastro-intestinal disturbances developed, which the patient speaks of as "being bilious." These spells consisted of vomiting, with cramp pains through the abdomen, and a diarrhea lasting

two or three days at a time. They followed closely indiscretions in diet, but the patient claims that there have been no recurrences during the past eight years.

Present History.—About two years ago (May, 1916), without previous warning of any kind, a very copious hemorrhage from the digestive tract occurred. A sudden feeling of great weakness was the first evidence of the trouble having been followed within a few hours by the passage of large and tarry evacuations from the bowels, which continued at intervals for four days. There was great pallor and other evidence typical of a severe hemorrhage.

A diagnosis of peptic ulcer, probably located in the duodenum, was made by the attending physician, and the customary bed rest with restricted diet was ordered, extending over a period of six weeks. The patient recovered from this attack without further incident and experienced no further trouble for six months. At the end of this period (October, 1916), there was a repetition of the previous hemorrhagic attack, again evidently from the upper intestine, but in somewhat less volume than before.

The case was again treated as one of simple peptic ulceration and, following his convalescence, another interval of six months intervened before the onset of the third hemorrhage.

This occurred in May, 1917, and proved to be more profuse than the preceding ones. On this occasion, the onset was characterized by the vomiting of a considerable quantity of clotted blood, followed shortly after by the passage of tarry stools.

I had the opportunity of seeing the patient for the first time four days after the onset of this attack, through the courtesy of Dr. Leo Burthe. At that time there was great prostration and a high degree of anemia (hemoglobin 60%; red cell count, 2,095,000, with a few erythroblasts).

The physical examination showed the patient to be of good physical development, with a tendency to obesity. No oedema or jaundice was noted. The heart was found to be enlarged slightly to the left, with a vigorous systolic impulse. No cardiac murmur could be detected. The surface arteries were moderately thickened. The pulse, full and rapid. The systolic pressure measured 170; diastolic, 100.

Nothing abnormal was found in the urine. Wassermann reaction was negative.

The abdomen showed normal contour without rigidities or sensitive areas. The liver and spleen could not be palpated.

Once more the patient was kept in bed for six weeks under greatly restricted diet. The occult blood reaction persisted in the stools for fully three weeks. However, there was a gradual return to the normal blood picture and the patient was, in fact, able to return to his business duties within two months. Since this time there has been a mild recurrence of the intestinal hemorrhage on one occasion (October, 1917). This did not necessitate the patient's returning to bed, however, nor did it interfere with his usual daily business routine.

The blood pressure readings in this case, between the intervals of the gastro-intestinal hemorrhages, have been persistently high, in spite of all plans of treatment directed towards its reduction. The highest systolic pressure recorded was 230 in December, 1917, and the minimum 190, in March of this year. He claims, notwithstanding, to feel entirely well, but looks forward with some anxiety to the completion of the next six months' period, when experience has taught him a hemorrhage into his gastro-intestinal tract might be expected.

A careful radiological examination of the entire digestive tract was made in this case within the past several weeks. A very small filling defect was found in the duodenal cap, immediately beyond the pyloric ring. This was visible alike under the fluoroscope and on the plates. It would be difficult to determine whether this defect represents, in fact, the scar of a healed duodenal ulceration, or that of a tissue break at the site of a previously ruptured duodenal vessel.

Even if we assume a true ulceration as the basis for the repeated hemorrhages in this case, the determining influence of the constant high blood pressure, to my mind, can scarcely be denied.

CASE III.—E. S., male, age 57, occupation, insurance agent.

Since the year 1913, this patient had been under the care of Dr. E. L. King and Dr. C. L. Eshleman of this city, to the latter of whom I am much indebted for the early notes of the case.

Previous Illness.—The patient had always been in good health, with the exception of one attack of continued fever, probably of malarial origin, which occurred during 1900 and lasted three months.

In 1909, application for life insurance was refused the patient, on the ground that his urine contained some albumen. He had exhibited no symptoms of kidney disease up to this time, however, and was inclined to pay little attention to this finding. Nevertheless, on the advice of his physician, he had tests of the urine made at subsequent intervals and was informed that albumen was constantly present. For several years back there had been a history of frequent urination at night, but this the patient attributed to the habit he had developed of drinking large quantities of water with his evening meal.

The patient had always been a heavy eater and acknowledged using alcohol to some excess. He likewise smoked excessively.

The physical examination of the patient, made in 1913 by Dr. Eshleman, showed a well-developed physique with a tendency to corpulence (average weight, 209 lbs.). A few slightly dilated venules on the nose and cheeks were noted. No diseased condition of the eye, nose or throat was found.

The heart was hypertrophied with the point of maximum intensity in the nipple line. The second aortic sound was accentuated, but no murmurs were present.

The superficial blood vessels were barely perceptible. Systolic pressure, 175.

The liver, normal in size. Spleen, not palpable. The abdomen

showed no evidence of portal stasis and was otherwise negative. Reflexes normal.

The urine examinations, made at frequent intervals, revealed a constant low specific gravity (1005-1010). The amount of moist albumen varied, but was never high. Occasionally hyaline casts could be demonstrated.

The first evidence of serious mischief in the patient's condition occurred in May, 1915. His health for several months previous had been unusually good, when suddenly he was seized with a fainting spell lasting several hours. Within a few hours, the cause of this was found to come from a large hemorrhage into the upper intestinal tract. The patient was confined to bed for several weeks, under treatment for a supposed peptic ulcer. After convalescence, the diagnosis of peptic ulcer was, in fact, confirmed by a radiologist, in the stage of quiescence or healing. This observation, however, may be open to doubt, as in the previous case, since a scar might easily be the result of a diffuse hemorrhage into the walls of the duodenum.

Following this attack, the health status of the patient remained unusually good for two years. He was able to follow his somewhat arduous work without stint and did not notice any digestive disturbance.

In the early part of 1917, however, warnings of a failing circulation began to show. He began to note dyspnoea, upon even moderate exertion, and had spells of air hunger at night. After eating, he likewise experienced a heaviness and fulness, with eructations but unaccompanied by pain.

On March 15, of this year, he was compelled to take to bed with a so-called attack of acute influenza, which proved to be the precursor of a series of events which finally terminated in his death, April 2, 1918. I saw him for the first time on March 21, in consultation with Dr. King. The gastro-intestinal symptoms had been most marked since the onset of the "grippe." We found him with a dilating heart, considerably cyanosed, and the "cold on the chest" we looked upon as a beginning pumonary oedema. Likewise, the digestive distress we regarded as secondary to the cardiac decompensation. His blood pressure measured 220 systolic with 105 diastolic. The urine showed a 2% moist albumen and many casts (Sp. Gr., 1025). A phenolsulphonephthalein test revealed poor kidney functioning (10%-12% respectively).

On March 27 a repetition of the attack of intestinal hemorrhage of three years before developed. This was most profuse in character and seemed to exhaust the patient completely. The arterial tension was markedly lowered at once. From this time to the date of his death, there was noted a gradual failure of the circulation, with rapid, irregular pulse, precordial pains and orthpnoea.

The stools remained dark red and tarry to the end.

Epicrisis.—In reviewing the clinical aspects of this case, it reveals the type commonly grouped as cardio-renal disease. The massive

intestinal hemorrhage, however, represents an interesting diversion from the usual clinical picture of this condition. It has seemed to me that these hemorrhages might best be explained by assuming for their basis an advanced arterial degeneration with an accompanying high blood tension.

This becomes all the more convincing when we consider the absence of all typical gastro-intestinal symptoms, which might denote the existence of an organic lesion within the digestive organs themselves.

The Various Causes Assigned as a Basis for Massive Gastro-Intestinal Hemorrhage.

Even in the earlier writings on medicine, references may be found to the occurrence of large hemorrhages from the upper digestive tract for which no adequate cause could be assigned. The term "gastric diapedesis" was used, in many instances, as a designation for this condition, a term which merely signified an oozing of blood from the gastric mucosa, without, however, explaining its cause.

In 1905, Hale White[1] collected, from his own experience, several examples of gastric hemorrhage of obscure origin, which he classified as instances of a simple "gastrostaxis." In the light of our more recent knowledge, an analysis of the etiology of these cases will show the indefinite status of this designation, since various diversified types can be identified among the group.

At the present time, the causes assigned as explanation for massive hemorrhage into the gastro-intestinal tract should, if possible, be based upon somewhat more specific and pathological grounds. A brief review and discussion of these various causes, as a means of throwing further light upon the cases reported above, it is thought might prove of especial value in this place.

1. *True Peptic Ulcer.*—(Cruveilhier ulceration.) The incidence of gross hemorrhage into the digestive tract, as a result of the common or Cruveilhier type of peptic ulcer, has been estimated variously. Lepert,[2] for example, in his series of cases, found the percentage of visible hemorrhage to be as low as 21, while Joslyn,[3] on the other hand, in the tabulation of his material, estimates the percentage as high as 81. Stockton's[4] statement that in peptic ulcer macroscopic hemorrhage occurs in approximately one-third of the cases is probably the more nearly correct view. Since further light has been thrown upon the more varied etiology of hemorrhagic effusions into the gastro-intestinal tract,

it would seem that peptic ulcer can no longer be considered to be as frequent a factor as was formerly held. Likewise, it is now recognized that particularly after the fourth decade the bleeding from an active peptic ulceration will be of more profuse character and will yield a higher percentage of fatality, because of the greater probability at this period of life of diseased states of the general arterial system.

2. *Exulceration Simplex.*—(Dieulafoy ulceration.) This condition was first described by Dieulafoy[5] in 1898, and its status as a definite clinical entity has been established subsequently by numerous observers. Quite recently Moschowitz[6] has presented a notable review of the entire available literature on the subject, adding four cases from his own experience that had come to operation, in each instance, with a previous diagnosis of true peptic ulcer.

The essential pathology of this type of ulceration would seem to partake of a superficial necrosis, involving principally the mucous layer of the stomach. The extensive bleeding has been found to occur, in most instances, from a rupture of a small arteriole in the submucosa. A definite etiological basis for the condition has, as yet, not been determined. Clinically, the course is marked by the sudden vomiting of blood, usually in large quantities, with the attending phenomena of pallor and shock. Only rarely do premonitory digestive symptoms occur. The prognosis is not an unfavorable one.

Malignant Growths.—Malignant growths invading the lumen of the digestive tract rarely become the cause of massive hemorrhages. Instead, there is to be expected rather a slow seepage of blood derived from capillary oozings. However, it should be remembered that the erosion of a large vessel might occur in neoplastic tissue, particularly in the presence of extensive ulceration.

Hepatic Cirrhosis.—This is universally recognized as among the more frequent sources of massive hemorrhage from the digestive tract.

According to the statistics collected by Preble[7] in 1900, among 60 cases of fatal gastro-intestinal hemorrhage in cirrhosis of the liver, in fully 85 per cent. the location of the ruptured varix was found to be in the lower third of the esophagus. In the remaining 15 per cent., which occurred into the stomach and

intestines, the copious bleeding was found to result, in a number of instances, from the simultaneous rupture of numerous capillaries in the mucosa.

Probably the most important feature of Preble's studies is embodied in his statement that "in two-thirds of the cases the diagnosis of hepatic cirrhosis cannot be made at all, or only after months or years, during which time other symptoms of cirrhosis have developed." This will serve to explain the occurrence of profuse hematemesis in certain cases for which no immediate cause is ascertainable.

Very recently, Hamburger[8] has reported an interesting case of profuse and recurring hematemesis with fatal outcome, which autopsy demonstrated had been caused by an extensive syphilitic cirrhosis of the liver.

Splenic Anemia and Other Forms of Splenomegaly.—The advent of hemorrhage into the stomach and intestinal tract in splenomegalies of whatever origin is by no means an uncommon clinical event. The most notable example of this is found in splenic anemia, or the so-called "Banti's disease." Whether Banti's disease as such should be considered a distinct clinical entity, still remains a matter of controversy. Quite recently, Norris, Symmers and Shapire[9] have insisted upon an entire elimination of the term from splenic pathology, claiming that the condition is merely a manifestation of a syphilitic involvement of the spleen and liver.

However, apart from the standpoint of etiology, the syndrome commonly known as Banti's disease is, as Osler has called attention to, not infrequently the basis of severe attacks of gastro-intestinal hemorrhage.

The fundamental cause of the hemorrhage cannot be definitely established in all of the cases, but it is not believed to be entirely dependent upon a cirrhosed liver, as some have claimed.

In an interesting case, reported by Donald C. Balfour[10] last year, recurring gastro-intestinal hemorrhages were present, for which no explanation could be found even after several exploratory laparotomies had been undertaken for the purpose. In the final effort to find some method of checking the persistent bleeding, Balfour decided upon a removal of the spleen, which indeed brought about prompt and complete recovery in the case. The spleen, after removal, was found to be twice its normal size,

and the liver, according to the records, showed "apparently moderate cirrhosis."

Toxic Hemorrhagic Gastritis.—This represents a pronounced grade of inflammation involving the gastric mucosa, as a result of a direct invasion of infectious organisms of various kinds, principally the streptococcus and the pneumococcus.

The source of such infection is usually found to be in one of the abdominal organs, though more remote antrums of infection, such as the tonsils, the gums and the root canals of the teeth, must be considered.

According to Deaver,[11] "a knowledge of the hemorrhagic possibilities of active congestion of the gastric mucosa cannot be learned at the mortuary slab, but only by witnessing its bleeding surface on the operating table in the living."

The recognition of this condition as one of the more common sources of sudden and massive hemorrhage from the stomach is of comparatively recent date. However, its status has now been fully established and in searching for the origin of an otherwise obscure gastrorhagia the possibility of a bleeding, inflamed gastric mucosa should not be overlooked.

An instructive case in point has recently been reported by Outland and Clendening.[12] The patient had suffered several attacks of severe gastric hemorrhage. Upon operation, the appendix was found buried in a dense mass of adhesions to which the omentum had become attached. The authors believe that the hemorrhage from the stomach, in this case, represented a seepage of blood from an infected gastric mucosa and that the infection itself had been conveyed directly from the appendix to the stomach by means of an adherent omentum.

The Blood Dyscrasias.—Profuse hemorrhage can occur in the course of a severe grade of anemia, as the result of the sudden rupture of a vessel wall which had been weakened by degenerative changes. The gastro-intestinal tract may thus become at times the scene of more or less copious hemorrhage as a sequel to such conditions as pernicious anemia, leukemia, Addison's disease, chronic malaria, etc. Likewise, in hemophilia and in the several forms of purpura, vascular accidents of a similar nature have been reported as occurring along the alimentary tract.

Aortic Aneurysms, with Rupture Into the Digestive Tract.—This is obviously among the less frequent causes of hemorrhage

into the digestive tract. Among the 149 instances of ruptured visceral aneurysms, tabulated by Nixon[13] in 1911, in only three did rupture occur directly into the gastro-intestinal tract. Since that time, four additional cases have been recorded in the literature, two of which, recently reported by Morlow (*Amer. Jour. Med. Science,* April, 1918) were found to have taken place directly into the duodenum.

Vicarious Menstruation.—The question still remains *sub-judice* as to whether a sudden and profuse hematemesis can be at any time explained solely upon the basis of a vicarious menstruation into the free lumen of the stomach.

In conjunction with many other careful observers, Stockton[14] takes his stand as a firm believer in the possibility of such an event. This author, in summarizing his views on the subject, clearly states his conviction that "the vomiting of blood in lieu of the catamenial discharge, is a reality."

On the other hand, Deaver[15] holds a decidedly contrary opinion, expressing himself emphatically in these terms: "Vicarious menstruation, as a cause of hematemesis, is an absurdity of the medical imagination more fertile in hypothesis than in knowledge of living pathology."

None the less, it would seem that the undoubted occurrence of vicarious menstruation in other organs would lend weight to the view that a similar event might take place, even though rarely, into the digestive tract.

The Role of the Arterial Factor in the Etiology of Massive Gastro-Intestinal Hemorrhage.—The assumption that localized disease of the gastric vessels themselves might take part in the pathogenesis of a peptic ulcer was entertained by Virchow, as far back as 1853. Even prior to that time, however, Cruveilhier already, in his earlier descriptions of the peptic ulcer lesion, had called attention to the sharply defined, discrete character of the lesion which he was inclined to explain upon the basis of some interferences with the vascular supply to the diseased area. In the more recent literature, scattered references can be found pointing to the effect of localized arterial disease as one of the factors predisposing to the production of peptic ulceration, particularly by Merkel, Hauser, Cohnheim, Payr, and others.

In 1913, this aspect of the subject received an exhaustive and critical anaylsis at the hands of Orphuls,[17] in an article entitled

"The Relation of Gastric and Duodenal Ulcer to Vascular Lesions." As a result of his study, this author expressed the view that gastric and duodenal ulcers arise uniformly from interference with the vascular supply to definitely limited areas of the gastric and duodenal mucosa. Numerous instances are cited by him, largely based upon material obtained by necropsy, to prove that arterio-sclerotic processes in particular with ensuing obliteration of the gastric and duodenal vessels become the determining factors in the etiology of peptic ulcer, especially in individuals past the age of thirty. While this extreme viewpoint has not met with general acceptance, increasing evidence is at hand to indicate to both clinician and pathologist that in the pathogenesis of peptic ulcer the arterio-sclerotic factor can no longer be considered as an entirely negligible one.

Stockton,[18] for example, in reviewing the records of a case of extensive gastric ulceration, seen by him, which was found at autopsy to have been caused by an obliterating arteritis of several of the gastric vessels, frankly acknowledges the possibility that, "the very large ulcers of the stomach occasionally observed past middle life result from the condition of arterial disease more often than is generally supposed."

In two of the cases reported above, it will be recalled that radiological examination indicated the presence of previous ulceration in the duodenum. Since both individuals likewise exhibited unmistakable evidence of arterial disease, it might be assumed that the profuse and recurring hemorrhages into the intestines, in each instance, had their source in an ulceration of arterio-sclerotic origin.

This could not be established definitely, however, in view of the lack of opportunity for direct inspection of the lesions themselves.

Apart from the possibility of the existence of a definite ulcerative lesion in each of the three cases, it is not to be denied that the associated hypertension of the arterial vessels played a most important role in determining the occurrence of the hemorrhagic attacks. With each recurring attack, a prompt lowering of the vascular tension was noted, as was to be expected, but, within a brief period the pressure readings showed a uniform and rapid return to the heights previously attained.

Under the circumstances, it has appeared to me as if the

copious effusion of blood, in these cases, served in a measure as a safety valve in blood-letting, relieving, in this manner, excessively high tension from the entire arterial system. We might even consider an apoplexy of this type within the free lumen of the digestive tract, as a life saving effort, sparing the more serious consequences which would await a vascular accident of similar nature in more vital organs.

Finally, it should not be overlooked that simple arterial rupture is possible along the gastro-intestinal tract, without previous ulceration, simulating a pathological picture not infrequently presented in other organs; notably, in the brain.

Under the strain of an increased vascular tension, the vessel wall, already weakened by ordinary degenerative changes, or by the previous formation of miliary aneurysms, may rupture outright with a consequent outpouring of blood.

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DISCUSSIONS.

DR. SEYMOUR BASCH, New York City: In these cases of gastro-intestinal hemorrhage we are so apt to diagnose a gastric and duodenal ulcer, that we overlook the fact that hemorrhage may occur with many other conditions. The question at issue involves the whole subject of gastrointestinal hemorrhage, and is too big to discuss fully; however, the differentiation between arterial disease conditions and ulcer has been well brought out by Dr. Simon. In the X-ray diagnosis in two of his cases, no conclusion was reached as to whether he was

dealing with a local process, as the result of arteriosclerosis, or with a primary ulcer. To illustrate the difficulty of this differentiation I would cite the case of a patient who came from Watertown, N. Y., several years ago, with a history very much like what Dr. Simon has narrated. He had gastric symptoms, and then a sudden profuse hemorrhage which ceased and later recurred. He was told that he had an ulcer, and advised to go to Johns Hopkins Hospital and be operated on. On his way he stopped in New York and consulted me. I found no sign that could lead me to definitely diagnose as ulcer. He had a very hard radial artery, and the X-ray showed the entire artery and the arch markedly sclerosed, proving beyond a doubt the existence of arteriosclerosis. His gastro-intestinal tract was also radiographed with a negative finding. He was given temporary rest and further arterio-sclerotic treatment, and has done well ever since.

Gastric ulcer is the most frequent cause of gastric hemorrhage, but not the only one; and we should not be hasty in making that diagnosis merely because a patient has a severe hemorrhage and seems to have an ulcer.

Dr. Charles D. Stockton, Buffalo, N. Y.: I wish to say that I have encountered on more than one occasion gastric hemorrhage as the result of diseased arteries, with and without the association of ulcer. In my book, I present a cut of a case that occurred in Buffalo, in which there showed in the center a sclerosed artery. I have seen this as the result of dissecting aneurism without any connection between the stomach and the aneurism. How the blood reached the stomach I could not tell. I have seen this bleeding from the stomach with diseased vessels or without diseased vessels, where you could find no blood in the stomach or oesophagus. I remember one case of bleeding at the cardia from a diseased artery. I remember a case that was very much like that of Dr. Friedenwald.

Dr. Lichty: The paper of Dr. Simon is before the Association for discussion.

Discussion of Dr. Simon's Paper.

Dr. Julius Friedenwald, Baltimore, Md.: Dr. Simon has presented a very interesting subject and one most important in diagnosis. That massive hemorrhages do occur independent of ulceration is well known. A case of this kind was under my care a few years ago. The patient, a man of seventy-two years of age, and highly arterio-sclerotic, was under treatment for cardiac disturbance and hypertention. There was little or no gastric or intestinal symptoms. One night after the patient had retired, he suddenly became nauseated and vomited an enormous quantity of blood and died in a few hours. At a partial autopsy the stomach was found filled with blood, the vessels much thickened, and a large rupture. No evidence whatsoever of ulceration could be observed.

Dr. Simon, closing: In line with Dr. Basch's remarks, I might say that in portions of the paper, which I did not have the opportunity to read this morning because of the lateness of the hour, the matter of the etiology of gastric hemorrhage in general was taken up and discussed in detail.

PART OF SYMPOSIUM ON CHRONIC DISEASES OF THE APPENDIX AND ASSOCIATED PATHOLOGICAL CONDITIONS.

Effect of Diseases of the Lower Bowel on the Rate of Emptying the Stomach.

By Franklin W. White, M. D.,

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It has been shown by Cannon and others that irritation of the colon may delay the emptying of the stomach. This is striking and well-known when powerful stimuli occur as in intestinal injury, in cutting, drying or handling the bowel. Here there is a definite protective mechanism holding back food above until some measure of healing occurs below.

Some men have also emphasized the effect of distension or irritation of the lower bowel by enemata, stasis in the ileum, inflammation of the appendix, adhesions in the ileocecal region, etc., in causing the stomach to empty slowly. (Hirsch,[1] Alvarez,[2] Baumstark,[3] Jordan,[4] Eisen,[5] Smithies,[6] Barclay,[7] Cole,[8] Ochsner,[9] Borbjarg.[10]) We have studied a group of such cases to find out how frequently this occurs and what sort of irritation gives this result. We have a series of clinical observations, and also of animal experiments.

Our results all point definitely the same way. First, regarding *frequency*—delay in emptying the stomach, is the exception, not the rule, in lesions of the lower bowel. Regarding the *kind of irritation*—a strong stimulus is needed from the lower bowel to slow the stomach.

Technique of Observations.

We judged the time of emptying the stomach by watching the progress of a barium meal with the Roentgen ray and fluorescent screen in men and cats. A carbohydrate meal was chosen because it favors prompt emptying of the stomach; we used potato gruel, mixed with barium sulphate, in the proportion of 100 grams of barium to 500 c.c. of gruel. We gave a 500 c.c. meal to the men

and 25 c.c. to the cats, and studied the residues in the stomach after five or six hours in men and after two or three hours in cats.

We tried to avoid other factors causing delay in emptying the stomach such as emotion, trauma, etc. For example, we might expect that fastening a cat to a holder, giving a meal by stomach tube, and then a rectal injection, would produce such unpleasant emotions that observation on the time of emptying the stomach would have little value. We used elderly female cats and found that with a little practice, these things could be deftly done within a few minutes, and the psychology of these cats is such that, if kindly treated, they were purring and contented within a minute or two after release from the holder. For later X-ray examinations no holder was needed.

Operative trauma, the use of a fistula or injections through the peritoneum into the bowel were avoided by simply passing a catheter per rectum through the colon up to the cecum and making injections through this; with the colon empty, and a catheter of proper size and flexibility (16 French), this is easily done under the fluorescent screen. Irritants to be injected were usually mixed with a little barium sulphate and the injection also made under the fluorescent screen to control how much was given and exactly where the injection was placed.

The Effect of Mechanical Filling or Distension of the Colon.

The men were given by mouth 500 c.c. of barium potato gruel. The cats were fed by stomach tube with 25 c.c. of the gruel. The cats were released at once and were not examined for two or three hours. In men bland rectal injections of 1,000 to 1,500 c.c. of potato gruel were given and retained as long as possible, usually from one to one and one-half hours. In cats a similar rectal injection of 30 to 40 c.c. was used.

This had little or no effect upon the emptying of the stomach. Food passed steadily through the pylorus while the enema was retained and the stomach was entirely empty within the normal period in each of the ten cases in which this was tried. The only effect was a slight delay in the action of the stomach for the first few minutes. This does not agree with the statement of Alvarez that introduction of food at the lower end of the

digestive tract markedly retards the progress of material coming down from above.

The fact that patients occasionally vomit after rectal feeding is poor evidence of reflex action from the colon to the stomach because rectal feeding is usually given on account of *previous* vomiting in gastric ulcer, stenosis, etc., and the fact remains that most patients do *not* vomit after rectal feeding.

The Effect of Stasis in Ileum.

Out of a group of more than two hundred patients in whom Roentgen observations were made six and twelve hours after a barium-potato gruel meal, there were 42 without important lesion of the stomach whose small intestines emptied slowly and who had residue in the ileum at the end of twelve or more hours. In sixteen, the twelve-hour ileal residue was large, in three cases persisting until 19, 48 and 54 hours respectively, in eighteen was moderate, and in eight small; the lesion was chronic appendicitis in twenty; adhesions of the ileum or colon in twenty, atony and ptosis in ten, disease of the gall-bladder in two.

Only four of these cases showed any delay in emptying the stomach as measured by a six-hour residue.

In two the stomach residue at the end of six hours was very small and both were delicate women over seventy in whom a slight delay was not remarkable. The other two with good-sized residue showed slight deformities near the pylorus, which we interpreted as possible adhesions or spasm.

In short in nearly all the cases which showed definite or marked delay in emptying the small intestine, the stomach emptied promptly. This does not seem to support Barclay's theory of an ileo-pyloric reflex from the last coils of the ileum to the pylorus to shut off the food supply by closing the pylorus until the ileum is more empty.

The pyloric spasm seen by radiologists in chronic appendicitis is variable and uncertain and has little constant effect on function, the more chronic and quiescent the appendix the less likely it is to cause delay.

Smithies found persistent gastric retention in only a little over 3 per cent. of pyloric spasms associated with appendicitis and cholecystitis; intermittent retention was frequent, and usually disappeared after removal of the appendix or gall-bladder.

Effect of Chemical Irritation of the Bowel.

This was tested in cats in the following way: In order to produce irritation in the cecum without any other trauma to the bowel, a well-oiled rectal catheter was passed up the colon to the cecum and the irritant injected with a syringe. The short simple colon of the cat makes it easy to pass a catheter and its exact location was shown with the fluorescent screen. Barium sulphate was mixed with the injected material so that the amount and place of the injection could be seen.

Twenty-five successive experiments with two different cats showed that injection of turpentine oil, either a few drops or ten drops, or 2 c.c., caused no delay in emptying the stomach. The same result was obtained with a few drops of croton oil. Injection of four or five drops of mixtures of mustard oil and olive oil gave varied results: in four instances the cat vomited the whole contents of the stomach promptly after the injections, in four cases the injection slowed the emptying of the stomach, evidently in proportion to the strength of the mustard oil, and the irritation produced in the colon. That is, the emptying time of the stomach was delayed from the normal two or three hours to five or six hours. In striking contrast to this, active irritation of the cecum with mustard oil caused *just as often* rapid downward emptying of the stomach and whole digestive tract, both above and below the irritated point.

We may grade the results roughly according to the degree of irritation of the cecum.

First.—Intense irritation caused prompt reverse peristalsis in the stomach with vomiting of its whole contents.

Second.—Marked irritation caused either (a) delay in emptying the stomach up to about twice the normal time, evidently due to spasm of the pylorus or (b) hyperperistalsis and rapid emptying of the stomach and whole digestive tract.

Third.—Moderate or slight irritation had no effect on the emptying of the stomach.

We did not get a perfect gradation of results, evidently because of the part played by spasm, which was very variable.

Clinical Data in Diseases of the Lower Bowel.

Data in the following group of intestinal cases show that delay in emptying the stomach after a barium meal is the exception

not the rule. We need to be careful in studying such a group to allow for some delay due to ptosis and atony of the stomach, which often occurs in thin, weak or old people.

In 7 cases of chronic colitis there was no delay in emptying the stomach. In 3 cases of tubercular ulceration of the colon there was no delay and the diseased part of the bowel was so irritable that the barium meal passed through it very rapidly, and it appeared empty. This is typical of this disease.

In 5 cancers of the colon, causing more or less obstruction, 2 of the cecum and ascending colon, 2 of the transverse colon and 1 of the sigmoid, there was no delay. In one case of chronic intussusception of the ileum one foot above the ileocecal valve there was no delay. Borbjarg, in studying tumors of the ileocecal region and colon using the residue six hours after a Rigel meal to test gastric motility, possibly an over delicate test), suggests that tumors below the cecum do not delay stomach emptying and that tumors in the ileocecal region frequently do.

We have seen that in 42 cases with ileal stasis occurring in chronic appendicitis and adhesions of the ileum and colon only 4 showed any delay in emptying the stomach. In an addition group of 53 cases, 27 with clear evidence of chronic changes about the appendix, 26 with adhesions of the ileum, cecum or colon, there were only 3 which showed any delay in emptying the stomach, one was a case of chronic appendicitis, two adhesions. There was one medium, two small five to six-hour residues.

We had little chance to study acute appendicitis because early operation is usually needed. Two out of eight cases of acute and subacute appendicitis showed slight delay in emptying the stomach, namely, a small six-hour residue, with the stomach empty at the end of seven or eight hours. This was not conclusive, as we obtained the same result in several other fever cases with pain, in which the bowel was not involved. Our experience with chemical irritants of the cecum suggest that different degrees of inflammation of the appendix may affect the stomach in a corresponding way, by causing vomiting, or delay in emptying, or rapid emptying, though we have not been able to prove it.

Peritoneal involvement is important. Compare the definite effect on the stomach which Cannon[11] got by performing a laparotomy and injecting croton oil into the cecum by needle through

the peritoneum, with the lack of effect we obtained by avoiding the peritoneum and injecting the croton oil by catheter. The element of pain is important—even such a simple lesion as fissure of the anus, if very painful, may cause delay, and a good-sized six-hour residue in the stomach.

In a total of 120 cases of lesions of the lower bowel there were only 9 or 7½ per cent. which showed any delay in emptying the stomach. Several of these cases were old and weak and some delay might be expected independent of reflexes from the lower bowel.

Clinical and experimental observation in lesions and irritation of the *upper* bowel (duodenum and jejunum) have shown that they often delay emptying of the stomach; they are outside the scope of this paper.

In conclusion, there is evidently a definite correlation of upper and lower parts of the digestive canal by a protective mechanism which works under a powerful stimulus such as intestinal injury or surgery or intense irritation, but which does not work under a moderate stimulus or simple mechanical condition. The action of this mechanism is complicated by the contrary results of spasm and hyperperistalsis.

Evidence indicates that the delay in emptying the stomach is the result of impulses through the vagus causing pylorospasm, not inhibition of the motor fibres of the stomach through the splanchnic nerves.

The delay in emptying the stomach caused by spasm of the pylorus is very variable, present one day and absent the next under similar conditions; in general, *marked delay* in emptying the stomach is far more often the result of actual lesions about the pylorus than of reflexes from the bowel.

It is not fair to compare the intestine to a railroad under a block system, where delay low down the line regularly holds up food for several blocks above or to say that "an irritating lesion slows the progress of food coming toward it from above." *It may or may not do so,* depending on the character and degree of the irritating lesion. It is evident that "stomach symptoms" in intestinal cases are not the result of slow emptying of the stomach as a rule, but are largely toxic or the result of referred pain or distress.

Summary.

The Roentgen ray method was used to study the effect of stimuli from the lower bowel on the rate of emptying of the stomach; the effect of mechanical filling and distension of the colon and enemata in men and cats; the effect of chemical irritation of the cecum in cats; the effect of diseases of the lower bowel in 120 cases of chronic colitis, tubercular ulceration and cancer of the colon, chronic and acute appendicitis and adhesions of the lower ileum and colon.

Our results all point the same way; first, delay in emptying the stomach is the exception, not the rule, in lesions of the lower bowel; second, a strong stimulus is needed from the lower bowel to slow the stomach, for it was found that the stomach emptied a barium meal within the normal time in some cases of ileal stasis of two or more days' duration and in most cases with good-sized twelve-hour residue in the ileum, also when the colon was distended with a large enema, also in most cases of chronic appendicitis and chronic inflammations and tumors of the colon.

Experiments on animals showed that when the colon was irritated by injections into the cecum variable results were obtained, intense irritation caused vomiting; less marked irritation caused either delay in emptying the stomach up to about twice the normal time, or rapid emptying of the stomach and whole digestive tract; moderate or slight irritation had no effect. The results were not perfectly graded, evidently because of variable spasm.

There is evidently a definite correlation of different parts of the digestive canal by a protective mechanism which works under a powerful stimulus, such as intestinal surgery or injury, or strong irritation, but which does not work under a moderate stimulus or simple mechanical condition. (The action of this mechanism is complicated by the contrary results of spasm and hyperperistalsis.)

Marked delay in emptying the stomach is far more often the result of actual lesions about the pylorus than of reflexes from the bowel. "Stomach symptoms" in intestinal cases are not as a rule the result of slow emptying of the stomach.

I wish to acknowledge my indebtedness to Prof. Walter B. Cannon, of Boston, for valuable help and suggestions, and to Dr. L. B. Morrison, of Boston, for Roentgen-ray data in some of the intestinal cases.

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SOME POINTS IN THE PATHOLOGY OF CHRONIC APPENDICITIS.

By Oskar Klotz,

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Chronic appendicitis in its various forms, offers an entirely different problem to the clinician and to the pathologist. To the former, the varying symptoms continued over indefinite periods of time, the absence of localizing manifestations and the not uncommon association of secondary nervous symptoms present difficulties in diagnosis hardly equalled by any other of the common diseases. The term chronicity, in the clinical sense, carries with it the meaning of time. The patient bears his complaint for months and years; often the complaint is neither greater nor less at his periodic visits to his physician, and in no sense cay we say that there is any evidence that the individual is suffering from a lesion which is progressive or in which the inflammatory process refuses to come to a conclusion. Distinctly, therefore, we are led to use the word "chronic" in relation to the time period during which the patient is complaining of symptoms, supposedly arising from a localized cause.

Chronic appendicitis to the pathologist has a meaning of another kind. He does not think of the condition in terms of symptoms, nor is he directly concerned whether the patient has suffered his discomfort for many months or years. The term to him implies a healed inflammatory lesion of the appendix which at some previous time had all the characters of an acute or sub-acute reaction. From this group we must separate the not uncommon cases of acute recurrent appendicitis, those individuals who have definite repeated or periodic acute exacerbations, during which there is a new inflammatory reaction similar to the preceding attack. Each of these acute exacerbations has its chronic phase, and if we were able to follow the histo-pathology of the individual lesions, they would bear a close similarity to each other and would pass through the same cycle in the process of inflammation. Hence the recurrent attacks tend towards cumulative

chronic lesions, which in their late and almost healed state do not illustrate the multiplicity of recurrence. We have repeatedly examined the appendix from cases of -socalled "chronic" appendicitis, to find evidence of an acute or sub-acute ulcer lying amidst tissue changes indicative of a former inflammation.

The rather divergent use of the term chronic appendicitis has to some extent prevented a common understanding between the clinician and pathologist. The internist in the clinical field has gained a conception of this malady through a group of symptoms, mainly of a subjective kind. The manifestations of the condition are not clear cut, and constitute no symptom complex. The surgical findings are equally indefinite. The appendix is found to be in different positions, at times being entirely retro-peritoneal; again adhesions are often present in greater or less extent; the appendix may be larger or smaller than normal; or a constriction may occupy its middle. In other words what is clinically described as chronic appendicitis has no definite group manifestations nor can a constant abnormal state be observed by the surgeon. The issue is almost equally confusing to the pathologist were he to attempt to offer a common pathological finding in explanation for the clinical findings and the clinical diagnosis of chronic appendicitis.

I might briefly illustrate this view by the laboratory findings obtained in quite a series of cases. Following the clinical diagnosis of chronic appendicitis, and here we must assume that the data for this diagnosis was carefully analyzed, our laboratory has classified the histological lesions as (1) recurrent appendicitis (with or without ulcer); (2) subacute appendicitis; (3) chronic ulcerative appendicitis; (4) chronic interstitial appendicitis; (5) chronic obliterative appendicitis; (6) chronic periappendicitis (adhesions). Associated with a number of these cases, concretions were found in the lumen of the appendix. Of a total 5,647 appendices examined, 1,718 showed chronic interstitial lesions, 1,689 had adhesions, 832 were obliterated and 195 had concretions. In our series we are unable to give statistical data associating the clinical findings with the pathological lesions; but we may add that we have examined not a few appendices which were removed with a diagnosis of chronic appendicitis, in which we were unable to demonstrate any affection about the appendix. The latter form a group of admitted mistaken diagnoses. To this group

we probably must add others, where although the appendix did show certain organic lesions classified as chronic appendicitis, the symptoms leading to the clinical diagnosis had their origin in causes outside the appendix, and were not removed by operative procedure upon the appendix. We have found that chronic interstitial appendicitis and chronic periappendicitis are about twice as frequent in women than men. They occur in greatest frequency betwen the ages of 20 and 40, but are also found in fair proportion of cases before and after this age. Chronic obliterative appendicitis, though falling in the highest frequency in the same age periods, is almost three times as frequent in women than in men. In partial explanation for the greater frequency in women we have the occasional association of the appendix in pelvic inflammatory processes. Operative procedure for the latter permits the surgeon to remove the appendix, which, for the symptoms arising from it, would not have been disturbed.

Age incidence of 2,368 cases of chronic appendicitis:

1-10	2.
11-20	15.4
21-30	38.6
31-40	28.5
41-50	11.6
51-60	2.6
61	1.1

An appreciation of chronic appendicitis may be gained by following the lesion from its beginning. The acute stage is one involving the mucosa in its crypts in ulceration. Such ulcers may be minute or large, superficial or deep, localized or spreading and may or may not be accompanied by symptoms indicating the appendiceal origin. There are very many instances of local lacunar appendicitis with ulceration in which the patient does not experience any severe discomfort; and such lesions may be repeated on several or many occasions before the cumulative effect of the inflammatory process upon the appendix brings about such change in its structure that the tissue derangement now manifests itself in certain vague symptoms. It is our belief that the great majority of cases of true chronic appendicitis have suffered repeated inflammatory lesions of the appendix, rather than that the

late effects are the result of a single acute attack. Moreover, we find no reason to change our view that appendicitis is of enterogenous origin and not a hematogenous infection. In fact, we can do no better than compare the mode of bacterial attack upon the appendix with the manner in which acute tonsillitis is brought about. Both appendix and tonsils are provided with lymphoid follicles which lie near the surface and have deep crypts lying between them. In these crypts bacterial fermentation leads to injury of the walls, commonly to erosion of the epithelium and the development of a shallow ulcer. The result of these lesions may be very minor or again it may progress to a severe clinical appendicitis with its sequelae. The minor attacks repair after an interval of a few days, but as with tonsillitis, there is prone to be a recurrence. It would appear that the tissues of the appendix become more susceptible than before the attack. Depending upon the nature and extent of each recurrence, definite changes in the architecture of the appendix are induced, these may be mainly found in a fibrosis of the sub-mucosa, a periappendicitis, or an obliteration of the lumen with destruction of the mucosa and its follicles. It is easily seen that the pathologist may not uncommonly meet with an ulcerating process of the appendix arising as a recurrent attack, when the clinical picture offers evidence only for a chronic appendicitis. In such instances. the acute lesions may give rise to no symptoms, while the damage induced in the appendix and other viscera through many former lesions causes symptoms of the so-called chronic appendicitis. Thus, too, we may meet with other inflammatory reactions in their sub-acute stages, while the clinical aspects suggest a chronic lesion.

It will bear repetition to state that acute appendicitis is much more common than would appear from the surgical statistics. Only a small proportion of the acute inflammatory reactions cause symptoms of sufficient severity to demand immediate surgical interference. Ulcers of the appendix which involve the mucosa alone are rarely recognized as such. In these respects again and in the lack of the relation of the symptoms to the lesion, the appendix bears a similarity to the tonsil.

From such varied findings in the appendix, we do not wonder that it is impossible to offer adequate explanation for the protean clinical picture. Pain, gastric disturbance, constipation and

altered alimentary secretions are often prominent sequelae which are lightly disposed of with the word "reflex." Just how and in what manner this reflex correlates responses from the appendix to the stomach or intestine or gall-bladder we can say very little. This much seems apparent, the frequency and severity of the symptoms is often parallel to the amount of peritoneal involvement. It is, however, also to be remembered that the symptoms of so-called chronic appendicitis arise to a large extent in the other abdominal viscera and have no relation whatever with lesions in the appendix. We have observed that a slow and progressive fibrosis of the submucosa of the appendix may lead to quite a marked architectural change, particularly where this occurs with advancing age; but in these cases it is rare to have any symptoms arise, and the condition is recognized only as an accidental finding at autopsy or operation. In these instances the peritoneum is not involved and the lesion was at no time an inflammatory one, but rather the result of a relative fibrosis accompanying the scleroses of old age. If we draw any deductions from these common senile changes, it would suggest that the mere presence of connective tissue in excess in the submucosa does not give rise to symptoms, while periappendicitis (adhesions) so commonly associated with true inflammatory processes in the appendix may be intimately associated with the clinical manifestations. Of the tissues of the appendix, the peritoneum is the most sensitive to pain, and also it may be, in conveying stimuli by its nerves and in a reflex arc to other abdominal viscera.

Various causes other than acute, subacute, and recurrent bacterial infection have been suggested for the development of chronic appendicitis. French authors have repeatedly called attention to the presence of worms in the appendix. The oxyuris is the most common of these parasites; but in America no great emphasis has been placed upon the presence of this worm in the appendix. It is possible that the frequency of this habitat has been underestimated, and that we may find some surprising results like those of Matsuoka, who in Edinburgh found worms or their ova in 48 out of 103 appendices removed at operation. The highest incidence of these parasites occurred between the ages of 10 and 30 years. From his study he was unable to assign any important role to the parasites in the production of appen-

dicitis, but he did observe that their presence was associated with symptoms simulating clinical appendicitis.

Other authors have suggested other factors as either inducing chronic appendicitis or manifestations like it. Steirlin found, in 61 cases operated upon, a mobile cecum. Of these 25 per cent. were males and 75 per cent. females. Sixty-seven per cent. occurred between the ages of fifteen and twenty-five years. The individual suffered colicky pains, constipation and discomfort in the right flank. Those cases which were only treated by removal of the appendix, did not do so well as when the cecum also received operative attention. In these cases it is claimed the pain is due to the effect of distention upon the sensitive nerves in the cecal wall. However, although these and other causes relating to anatomical aberrations have a place in the discussion of the etiology of chronic appendicitis, they bear no prime importance in the majority of cases. Whether in the usual mode of production, a particular micro-organism is more commonly the infecting agent, we do not know. It has been suggested that the viridans group of streptococci possess the qualities for inducing low grade and recurrent tissue lesions, and that in the appendix as in the tissues of the pharynx, this bacterium plays the chief role. This may well be, particularly as this group has various of its members constantly present in the bowel. Nevertheless other bacteria may at times play an equally important part, and there is no evidence that the initial damage may not arise from various bacteria normally present as well as organisms not usually found in these parts.

It is of interest in respect to the bacterial flora of the intestine that the character of the diet has an influence in increasing or decreasing the number of certain organisms. If a particular kind of diet is in any way associated with the incidence of acute or chronic appendicitis, this is probably through its influence in allowing particular types of bacteria to thrive and injure certain parts of the bowel.

Finally, if it be true that chronic appendicitis is a very variable clinical and pathological condition, sometimes appearing alone, but also occurring in association with other intestinal lesions or it may be in association with lesions of other organs, it is important to appreciate that the symptoms may be widely di-

vergent and also that an operation upon the appendix does not necessarily relieve the patient of all of the symptoms. Not infrequently the associated pathological process in other abdominal viscera continues to provoke the symptoms which were diagnosed as chronic appendicitis.

THE ROENTGEN RAYS IN THE DIAGNOSIS OF APPENDICITIS.*

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In the great majority of these cases the Roentgen rays are not necessary for the diagnosis of appendicitis. This is especially true in acute appendicitis. In chronic appendicitis, however, the symptoms are very often obscure and the clinical signs and other evidences of an inflamed appendix are indefinite or are complicated by lesions in other organs. In these obscure cases the Roentgen rays will give the greatest assistance in making such diagnosis.

Acute Appendicitis.—In acute appendicitis the Roentgen rays are very rarely necessary to assist in the diagnosis, but at least two points of diagnostic value can be demonstrated in these cases. 1. In that group of patients in which there are symptoms of acute appendicitis due to an early pneumonia developing in the lower lobe of the right lung, the Roentgen rays will be useful in demonstrating the lesion in the lung, and thereby aid in differentiating pneumonia from appendicitis. 2. A valuable point in the diagnosis of acute appendicitis brought out by Case is obtained by filling the colon to demonstrate the relations of the area of acute tenderness, and thereby assist in differentiating appendicitis from other affections of the organs in the right lower quadrant of the abdomen.

Chronic Appendicitis.—The chronic appendix gives much Roentgen evidence of value in diagnosis. In the great majority of instances the patients sent to me for study, in which I find chronic appendicitis, are referred because of obscure stomach symptoms, in which the diagnosis of gastric ulcer is suspected, but in which the evidence is insufficient for an operation, or in other cases the gall-bladder or duodenum are under suspicion, but it is my opinion that in all this group of cases in which the symptoms are variable and may refer to the stomach, the duod-

*Read by invitation before the American Gastro-Enterological Association at Atlantic City, May 6, 1918.

enum, the gall-bladder, the kidneys, the appendix or the bowel, that nothing short of a complete Roentgen examination of the entire gastro-intestinal tract, including the gall-bladder, and at times even the urinary tract should be made in order to reach a definite diagnosis. I cannot insist too strongly upon this point. Otherwise important evidence will be overlooked, for one may find more than one organ involved, or the affected organ may be overlooked entirely. If any of these organs are studied separately, and nothing is found, the patient has not been benefited; his symptoms continue; no diagnosis is made, and generally he becomes disgusted with the physician and with the methods used in diagnosis, which is a detriment to everyone.

Technique.—In this general group of cases, therefore, it is my practice to order for the patient a purgative, such as a bottle of citrate of magnesia at nine o'clock on the night preceding the examination. The patient then reports at nine o'clock the following morning without breakfast, at which time a thorough study of the gall-bladder region is made, using six or eight plates. The patient is then viewed fluoroscopically, at which time any gross abnormalities in the chest are noticed; the abdomen is viewed in general, at which time occasionally a biliary calculus or a urinary calculus may be observed before giving the opaque meal. At times even a urinary calculus will give rise to these obscure gastro-intestinal symptoms. The patient is then given a barium meal consisting of approximately two ounces of barium in a pint of buttermilk, or one of the prepared fermented milks. This makes an excellent vehicle, as was originally demonstrated by me in 1907.[1] A careful study is then made of the stomach and duodenum, and, if anything abnormal is found, the patient is again seen in either three or four or six hours, depending upon the conditions. If nothing abnormal is observed at the first visit, by a careful fluoroscopic examination, the patient is again seen at the end of eight hours, at which time the opaque material has entered the cecum and ascending colon, and one can make some of the preliminary studies with reference to the terminal portion of the ileum, the cecum, and, occasionally at this time, the appendix will be visualized. At times this is the only occasion at which the appendix can be demonstrated. Generally at this eight-hour period the appendix is not filled. The patient is next seen at the end of twenty-four hours from the first visit,

at which time, in practically all instances, the cecum and ascending colon are well demonstrated, and, in the great majority of instances, the appendix can be demonstrated. The patient is allowed to continue with regular meals, after the first barium meal, unless something is found in the stomach or duodenum. No purgative is allowed during the entire study. At the twenty-four hour examinations, studies are made with reference to the cecal region and the entire colon. The patient is next seen at the end of forty-eight hours, at which time further observations are made with reference to the ileocecal region, and the filling effect throughout the colon, and then the patient is given a barium enema. This outlines the colon and further demonstrates its relation to other organs, as well as its relation to the appendix. It also enables one to recognize any constriction or filling defect, and the patient does not have the objectionable drying up of hard barium masses, which sometimes gives trouble in their expulsion from the rectum.

The diagnostic points obtained through roentgenology are:

1. *Localized Tenderness.*—This is the most valuable sign obtained, and is elicited either by direct palpation under the screen by means of the gloved hand, or much better (which is my practice), by means of a wooden spoon-like instrument, called a "distinctor." This wooden spoon can be passed readily under the screen and is controlled by the hand above the screen over the protection of the lead glass, and if this spoon is surrounded by a rim of metal, one can easily move it around over the different parts of the colon, and different parts of the abdomen, and by watching the ring can definitely localize the tenderness of appendicitis in the cecal region, or over the appendix wherever it may be located. When the appendix is visualized (that is, when the barium meal enters the appendix so that it can be distinctly seen), one can often localize the tenderness directly over the appendix, and when the appendix is movable not infrequently the localized tenderness moves with the appendix. I have been able, in a number of cases, to move the appendix as much as three or four inches, and in each instance the sharply localized tenderness moved with the appendix. This may seem contradictory or inconsistent with some of the ideas of the sensibility of the viscera, but whether contradictory or inconsistent, it is a fact. Without suggesting to the patient, I have been able to move

my wooden spoon around over the abdomen, and in each instance, when I came back to the location of the appendix, the patient complained of pain, even though I had moved the appendix from its original place. This tenderness is persistent and is present throughout the various studies made. At times this tenderness is acute, and sharply localized, and at others is more or less general, and less acute. A vague tenderness is more likely when the appendix is retro-cecal, in which instace there is considerable soreness, but the tenderness is not sharply localized until one twists the patient in such a manner as to bring the pressure directly to bear upon the appendix, in which instance it is often quite acute. If no tenderness is present and if at the same time the cecum is freely movable, I believe that one can say that no appendicitis exists. If, on the other hand, there is localized tenderness over the cecum, with fixation of the cecum, and no visualization of the appendix, it very frequently means an obliteration of the appendix by inflammatory exudate, which prevents the appendix from filling with the barium meal. Localized tenderness, with fixation of the cecum, and without filling defect, I believe, is strong evidence of appendicitis. Clinically the surgeon and physician are apt to look for tenderness over McBurney's point. As we have many opportunities of studying the position of the appendix and the localized tenderness, we realize how much in error we may be if we depend upon localized tenderness over McBurney's point, as evidence of chronic appendicitis. For example, if the appendix is located deep in the pelvis, there will be absolutely no tenderness over McBurney's point. Likewise, if the appendix is located in the hepatic region, and very commonly when the appendix is retrocecal, there is no localized tenderness over McBurney's point. Then, too, the appendix may be on the left side instead of the right, either due to non-rotation of the colon or to complete transposition of the viscera.

2. *Demonstration of the Appendix.*—The appendix can occasionally be demonstrated by the opaque enema, but in many more instances it is demonstrated by means of the opaque meal, particularly when administered with buttermilk. Case reported a demonstrable appendix in 273 out of 763 cases which were referred because of gastro-intestinal symptoms. George and Gerber have succeeded in demonstrating the appendix, either normal

or pathological, in 7 out of every 10 cases. Quimby in 141 cases was able to obtain sufficient data to determine the condition and the position of the appendix in 90 per cent. of them. The remaining 10 per cent. were those in which the position of the cecum prohibited a thorough inspection. I believe that in the majority of cases referred for gastro-intestinal study in which the barium and buttermilk meal is administered, the appendix can be demonstrated if one looks for it at the end of eight hours, at the end of twenty-four hours, and at the end of forty-eight hours. It is not always visualized in a plate made of this region, but if one palpates the cecum by means of the wooden spoon or "distinctor," if the appendix has been filled with the barium, it can, I believe, always be demonstrated, even if it is lying behind the cecum. To accomplish this, one should rotate the patient to the right or to the left sufficient to bring the posterior surface of the cecum into view; the appendix can then be demonstrated if it is filled with opaque material. I believe that no case is thoroughly studied unless this procedure is followed. Regarding the significance of bismuth fillings of the appendix, Skinner, after reviewing the literature on the subject states that there is no agreement. At one extreme we find Groedel stating that the ability to demonstrate the opaque filled appendix is a sufficient basis for accusing it of being pathological. Case is inclined to the view that the appendix which can be filled with bismuth, if not definitely pathological, it is at least potentially dangerous. George and Gerber agree with Case in those cases where bismuth remains in the appendix forty-eight hours or more after it has passed out of the contiguous intestinal tract, while Imboden states that the mere presence of some of the opaque material still in the appendix is no indication of chronic disease. Cohen says that fecal contents enter normally into the appendix.

3. *Fixation.*—A chronically inflamed appendix is very apt to become more or less attached to the surrounding tissues. It may be only attached at its tip, in which instance the greater portion of the appendix could be moved around freely, together with the cecum, and yet the tip of the appendix remain in a stationary position. On the other hand, the appendix may be fixed throughout, or it may be fixed at its base, and the tip of the appendix may be movable. However, absence of fixation, or evidence of adhesions about the appendix must not be regarded as negative

evidence in the diagnosis of chronic appendicitis, for we all know that an appendix may be inflamed and yet be freely movable. In this instance, the localized tenderness again is of most value.

4. *Position of the Appendix.*—Normally the appendix is directed downward into the pelvis, but normally it is freely movable, and changes its position without external influence to a considerable extent during twenty-four or forty-eight hours. It not only changes its position but its shape, indicating that there is likely some vermicular or peristaltic movement associated with the appendix. One may find, therefore, a chronic appendix in a normal position lying in the pelvis, or lying transverse, or lying along the inner side of the ascending colon, or it may be retro-cecal, or, as in one case of mine, the appendix was wound around the pyloric end of the stomach. In a number of instances I have found it up in the gall-bladder region, in which instances the patients are generally sent for a gall-bladder examination rather than an appendiceal study. In general, when the appendix is directed upwards or is retro-cecal it is more likely to indicate chronic appendicitis.

5. *Kinking or Angulation of the Appendix.*—The mere bending of the appendix has no significance, for the shape of the appendix will vary many times within twenty-four hours, but if there is a fixed angulation it is very commonly due to an adhesion at the point of fixation. This has distinct significance.

6. *Constriction.*—Constriction, or dilatation, or irregularities in the lumen. These may consist of a bulbous portion, or the whole appendix may be much dilated, or one may have marked irregularity in the lumen. All of these, I believe, have pathological significance.

7. *Abnormal Retention.*—If the appendix remains filled with barium after the cecum and ascending colon have become empty, or after the entire colon is emptied, I believe that it has pathological significance. On this point I am in accord with opinions expressed by Case, George and Gerber, and Imboden.

8. *Incompetent Ileo-Cecal Valve.*—The incompetency of the ileo-cecal valve can often be recognized by the fact that, at the end of twenty-four hours after givng an opaque meal, the ileum is usually entirely empty, and yet at the end of thirty-six or forty-eight hours the terminal portion of the ileum may contain some

of the opaque material. This surely means, and is the best demonstrable proof of incompetency of the ileo-cecal valve. It is due to regurgitation of the contents of the colon into the ileum, and is probably carried there by reversed peristalsis.

Other Roentgenological Evidence of Pathology in the Right Lower Quadrant of the Abdomen.

1. *Enteroliths in the Cecum,* such as was demonstrated in the case reported by Stamm and myself.[2] In one of these cases the enterolith consisted of a fecal mass, globular-shaped, about an inch and a half in diameter, and movable between the cecum and several inches higher in the ascending colon. It gave rise to pain in the right iliac fossa, and also was associated with recurring attacks of diarrhea. It was finally carried to the rectum, after many glycerine enemas, and was removed digitally from the rectum by the attending physician at the end of two months.

2. *Adhesions of the Cecum to the Side of the Rectum,* is illustrated by the case of a young man who for twenty years suffered with constipation, but at the same time had constant desire for stool, and yet, no matter how often he emptied his bowels, he still had the desire for further rectal expulsion. This symptom was found to be due to a dilated cecum attached to the rectum, which, becoming distended with fecal matter, pressed upon the rectum, gave the patient a desire for stool, and the patient was continually making the effort to expel the cecum through his rectum, without success, of course. This patient was relieved by operation.

3. *Carcinoma of the Cecum.*—Carcinoma of the cecum is associated with two of the most important Roentgenological symptoms of chronic appendicitis, namely, localized tenderness and fixation, but one can differentiate these because of the filling defect in the cecum due to the carcinoma. This filling defect is practically always absent in connection with chronic appendicitis, excepting when a large appendiceal abscess is present, which produces a pressure defect. The pressure defect can be differentiated by the smooth rather than the serrated outline.

4. *Psoas Abscess or Iliac Abscess,* which ultimately points to the neighborhood of Poupart's ligament, may give rise to localized tenderness, and a great deal of pain and distress, and the consideration of chronic appendicitis is often forced upon us.

In these cases an examination of the spinal column will help to clear the diagnosis, and generally the cecum and appendix are found to be freely movable unless there is associated chronic appendicitis. The two conditions may, of course, be present at the same time.

6. *Urinary Calculus.*—I have seen several cases operated upon for chronic appendicitis, when a subsequent Roentgen examination demonstrated the presence of a ureteral calculus. Even renal calculus may give reflected pains in the right quadrant of the abdomen.

Conclusions.

1. Chronic appendicitis commonly gives obscure symptoms.
2. A complete and careful Roentgenological study will give valuable evidence in all cases.
3. A definite diagnosis, either positive or negative, can be made in the majority of cases.

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VISCEROPTOSIS AND CHRONIC APPENDICITIS.

By Thomas R. Brown.

Others have already touched upon the many cases of chronic appendicitis secondary to acute or subacute inflammation of this organ, cases in which in many instances a most careful history running back into early childhood may be necessary to disclose that there were acute conditions ever present—long forgotten attacks of pain in the right side or repeated attacks of colic in childhood or even babyhood, only discovered after very careful questioning, being the only obvious expressions of acute appendical inflammation. Even in this group of cases, when the acute stage is a thing of the past and when the only symptoms remaining are those both local and reflex due to cecal stasis, thickened and twisted appendix, it is extremely problematic as to the wisdom of suggesting surgical treatment—as many of us have too often discovered to our cost.

But we wish here to discuss a different type of chronic appendical and periappendical inflammation, a type chronic from the first, with no acute stage, met with peculiar frequency in high grades of visceroptosis. In the first place, that there is a definite relationship between visceroptosis and chronic appendicitis seems to us to be beyond peradventure, and yet it is very likely to be misinterpreted. Our feeling has been that in this group of cases the appendicitis is in no sense primary, but simply represents one phase of a low-grade inflammatory process, of which perityphlitis, pericolitis, and possibly such conditions as Jackson's veil or Lane's band are other manifestations, an inflammation probably brought about by disturbances of blood and lymph supply inevitable to such high grades of displacement, with, as a possible additional factor, a low grade of toxemia or bacteremia due to the stasis and fecal retention. The real tragedy in these cases is the usual lack of realization that this appendical inflammation is but a part of this low-grade inflammatory process involving not only the appendix, but the terminal ileum, cecum, ascending colon, and sometimes even the first portion of the transverse colon, and, not realizing this relationship, the unfortunate tendency of so many physicians to ascribe all the symp-

toms to the chronic appendicitis, so easily recognized by local signs and symptoms and by fluoroscopic study, and with its discovery urging operative removal in the belief that by so doing the symptoms may be relieved—a dream that is rarely realized, a chimera that too soon fades away with the return of many or all of the original symptoms.

Our feeling has always been that in high grades of visceroptosis with fecal stasis, in which the appendix can be proved to be definitely diseased, it is, as a rule, worse than useless to remove it, for the postoperative adhesions which usually form, though, of course, lessened by the better surgical care now in vogue in many hospitals, often lead to an increase in fecal retention and a diminution in lower bowel tone and peristalsis that makes the second state of that man—or oftener woman—worse than the first. After all, to expect the removal of what is but an effect and not the primary cause to clear up a picture in the development of which disturbances—secretory, motor, and sensory—of the gut play important rôles, as well as marked variations from the normal intestinal bacteriology, is chimeric to say the least. And so let us not be too optimistic when, after fluoroscopic examination or X-ray plate, the patient is told that he has a chronic appendicitis with visceroptosis, and that the appendical removal will be all-healing in its effects. The surgeon who removes the often comparatively quite innocent organ and then sees the patient no more may have this delusion, but not the medical man to whom the patient so often returns in three or six months with the same complaints. We should not like to say how many patients we have seen during the past few years in whom after appendectomy the symptoms, both local and reflex, have returned —the cecal stasis, the pericecal thickening on the one hand, the hyperesthenic stomach with pylorospasm, hyperchlorhydria, or hyperchylia on the other. It is but another example of the all too frequent tendency of the day to attempt to explain all the symptoms of any case by the one organ or tissue found diseased, and to expect its removal to bring about a cure.

DISCUSSIONS.

DR. S. J. MELTZER, New York City: Pardon me, Mr. President, for attempting to take part in the discussion. Just now I am interested in resuscitation; I wish to resuscitate something. Sometime ago a physician, who heard my name, asked me if I am the man of the

"Meltzer" sign in chronic appendicitis. Some of you probably remember that about sixteen years ago I read a paper before this Society on the value of using the voluntary contraction of the iliopsoas muscle (by having the patient raise his right leg while palpating the region of the appendix) as a means of diagnosis in appendicitis. I am not going to read this paper again; I am merely trying to resuscitate it. Someone, perhaps, may hunt it up and read it.

DR. GERSTER: We all know it and use it.

DR. MELZER: I did not hear it mentioned in the discussion and therefore referred to it.

Perhaps I may make a few other brief remarks.

I used to tell patients whom I had advised to have their appendix removed; *you have no idea what a pleasure it is to have a good stomach ache, without having to fear that it may mean a serious case of appendicitis.* This psychological factor deserves to have a place in the considerations, when advising an operation for appendicitis.

I believe that Dr. Kaufmann is right in what he says; mild appendicitis may be merely a part of a general colitis. But it may be a part in a vicious circle, and by removing one link of it you may bring about a final cure.

I wish at the same time to direct your attention to a grave aspect which apparently innocent operations for chronic appendicitis may occasionally present, and which I have not heard mentioned in the discussion. Many years ago I met my friend Dr. Joseph Blake looking downcast on that day. He told me the reason for it. "Nine days ago, I removed a practically normal appendix from a friend of mine; this morning, he died. I do not know the cause of his death." Some years later Dr. Blake came nearly dying after an interval operation for appendicitis—from pulmonary embolism. This grave incident seems to complicate sometimes innocent and aseptic operations in the lower quadrant of the abdomen. I believe that some years ago Dr. Gibson collected 130 cases of this kind. The mechanism of this grave complication is not yet understood; I believe that the problem has not even been properly studied.

DR. LUDWIG KAST, New York City: It is impossible to go further into details, in the short time of fifteen minutes. The whole symposium might have been taken up with any one of the questions raised in the discussion.

As to the problem of Dr. Combe's treatment, I can answer clearly. The question seems raised between the treatment of Dr. Combe or Dr. von Noorden. The latter had the idea of putting into the digestive tract a lot of residual matter for the intestines. Many cases can be cured by this treatment in a few weeks, but these are cases in which there is no serious infection, nor serious retention. Other cases with serious infections do badly with that treatment. They suffer with pain, gas distention and reflectory derangement of the stomach. For

such cases the treatment along the line of Dr. Combe seems more appropriate.

As to the sloppy meals, we know all along of course that many digestive symptoms are aggravated by large amount of fluid taken with meals. Cases of atony of the stomach and tendency to retention in the ascending colon should separate eating and drinking. Often a few days of dry meals will suffice to bring about marked improvement, in the functional efficiency of the colon. The patients must, of course, get sufficient fluid, however, they should not get it with their meals.

A point of great importance is the relation of the endrocrine system to the digestive functions. It is a subject of vast importance and of far-reaching effect. If we consider only the effect of the endocrine system upon the nonstriated muscle fibres of the intestines we can realize how much its influence is over the rate of propulsion of intestinal contents and indirectly over their chemistry. The motility rests largely upon tone and the tone rests largely upon the endocrine systm.

Dr. Oskar Klotz, Pittsburgh, Pa.: There is one point of importance which is emphasized in listening to the discussion to which I should like to refer, and it is this, that the term chronic appendicitis is misunderstood and improperly applied by not a few individuals. This is apparent in the preceding discussions when different speakers have used the term in referring to conditions quite aside from the appendix. The misapplication of the term has arisen through its use by the clinician in indicating clinical symptoms which experience has shown simulate those of chronic appendicitis. But this gives no right for its application in diseases of colon, gall bladder or small intestine. We only delay a proper and co-ordinate understanding of chronic appendicitis by arguing the topic from impossible standpoints.

In as much as lesions in the appendix may be associated with disease in neighboring or distant organs, I believe that we should be open to realize that a variety of factors may be important in the cause. We will probably fail in finding a single agent which alone is responsible for the inflammatory state of the appendix. We must also be ready to appreciate that there are anatomical and other states which may predispose the appendix to injury. Such a predisposition may also arise through a functional relation with other organs.

Dr. Thomas R. Brown, Baltimore, Md., closing: I should like to say two or three things. With regard to Dr. White's point, I may say that I have been frequently struck with a definite demonstration of reversed action of which he speaks. Dr. Finney, could produce a pylorospasm, by pinching the cecum. This suggests that stretching of the peritoneum is probably at the basis of it.

In Dr. Pfahler's demonstration, he did not call attention to a fact which we have used in our fluoroscopic examination. In some cases, we have to use a method that is rapid. We give bismuth eighteen hours before the examination, and then, again just before it. We

can study both stomach and intestines at the same time. We have been struck by the cecal stasis, and the fact that the stomach is pulled downward and to the right. Operation, in these cases does not show any adhesion of the appendix and stomach, and we attributed the picture to the fact that the omentum is the tissue which migrates toward inflammation. There is a pull down on the stomach, which is rather characteristic in these fluoroscopic examinations. We feel that it is of great value to us.

I should like to ask Dr. Kast how he feels regarding Combe's views about intestinal bacteriology. He does not go as deeply as I should like into the dietetics of infection, or say how large a role he gives to the elimination of meat from the diet in these cases.

Regarding the question of surgical treatment, I wish to protest against this humility on the part of the surgeon. Dr. Draper assumes that it is the surgeon who has been blamed, if things go wrong. I feel that patients would rather run the risk of serious consequences than wait for the slower medical results.

I wish also to protest against the idea that there must be gross changes, or there is nothing wrong. I do not think that anyone who has studied stomach conditions can fail to realize the fact that a superficial erosion may do as much functional harm as a deep callous ulcer. It is essential to realize that the great progress in medicine in the handling of these cases lies in a much more refined study of the cases, and possibly of the bacteriology of the whole gastrointestinal tract. There are many questions of secretions and hormones involved. Why, for instance, do we meet with a thin walled duodenum in cases of chronic pancreatitis? We do not know.

Dr. Franklin W. White, Boston, Mass. (closing): I do not know whether Dr. Bryant's remarks were *apropos* of my paper or not. Of course a gastrocolic reflex is a well known fact. As soon as you put something into the stomach, things in the ileum begin to move along. I have tried to find out whether or not there was a reflex which worked the other way, namely an ileo gastric reflex.

There are evidently two groups of cases with conditions in the cecum. There is an infectious group, where we have not only the appendix but the colon also, really infected, and there is a stasis group, in which we have the cecum dilated and holding material for a long time, but in which there is practically no infection discoverable. I say that, because I have observed a series of cases at the Massachusetts General Hospital, with reference to epilepsy. The right colon, or a considerable portion of it, was taken out, and the specimens showed no infection and practically no pathology in spite of the fact that there had been long delay of material in that side of the colon.

With reference to the X-ray examination, we must compare the findings with the normal findings. In regard to the mobility or fixity of the cecum or appendix, I find that there is a very considerable

normal difference to be observed in different patients before the fluorescent screen. There is a difference in the length of the mesentery. In some cases, this part of the bowel is normally fixed, and in others, it is mobile.

I wish that some of the clinicians would say something about the value of cecostomy in these intestinal stasis cases.

DR. FRANKLIN W. WHITE, Boston, Mass.: I should like to say a word about the paper of Dr. Einhorn. My series of cases has been a good deal smaller than Dr. Einhorn's and distinctly smaller than Dr. Brown's, but I met certain facts in this small group which impressed me. We found that even where we got clear bile from the duodenum, gall stones were occasionally found, that if the duodenal contents were decidedly cloudy, we could expect to find cholecystitis, either with or without stones.

Dr. Hemmeter mentioned a case of ulcer with cloudy duodenal contents. We found a similar case.

Pancreatic cases are a more difficult class to deal with. We have much difficulty in making the diagnosis of early pancreatic disease by any method, and we should welcome any new one that will help. This method should be tried, for that reason. The series in which I have examined the duodenal contents includes twelve cases with cancer of the pancreas or chronic pancreatitis, and we met two types of difficulties. One is inherent in the nature of the ferment test. Ferments are peculiar things, as anyone will realize who has tested them, and we felt that we could only detect *marked* changes in the ferments by our ferment tests. I noticed in Dr. Einhorn's earlier papers, that the Mett's tubes were used to estimate trypsin. They proved so unsatisfactory in our hands that we used the Gross-Fuld method, to which Dr. Brown referred, which seemed to be a great deal more accurate.

The other difficulty is, that well marked pancreatic disease may be present and still we may get no change in secretion owing to compensatory activity of the rest of the gland. In the marked pancreatic cases, the stools, with the general examination and history, led us to our diagnosis, but in the cases of moderate grade, where our difficulties in diagnosis begin, the use of the duodenal contents was rather unsatisfactory. The method does give valuable evidence at times and is worthy of a trial, we need more results, before we can be sure of it.

DR. FRANKLIN W. WHITE, Boston, Mass.: It struck me in listening to Dr. Hemmeter's remarks about estimating the total dry residue of the duodenal contents as a means of deciding about the presence of cholecystitis or gall stones, that in such a complicated mixture as the duodenal juice, consisting of several secretions containing both organic and inorganic substances, there would probably be other variables beside the calcium salts and bile salts, which would complicate the results a good deal.

Dr. Arpad G. Gerster, New York City: Though honored by its membership, I have always considered myself a mere guest of this Association, hence have avoided as much as possible to inflict upon you the airing of purely surgical matters. But this symposium was concluded by a surgical paper. I beg, therefore, to be permitted to open the discussion by a few surgical remarks. You all remember what a lucrative industry became the removal of the vermiform appendix, say twenty or twenty-five years ago. An analagous phenomenon was the craze, to remove the appendages of the uterus; thirty-five or forty years ago the tonsils were looked upon as the cause of all sorts of recondite maladies. The important thing is this, that disturbances of remote functions were explained by irregularities, often of the minutest anatomical significance, of this or that special organ. The assertion was not early met with that functional disorders of the stomach, the biliary system and the small and large intestine were cured by the removal of the appendix, which itself showed little or no evidence of pathological change. An obliterated appendix, an organ which had become practically extinct, was just as readily accepted as the source of all evil, as one which showed marked changes due to former acute or subacute attacks. Some remnants of this view of things are still persistent, and maintain themselves through the force of the discredited but still potent rule: "*Post hoc ergo propter hoc.*" It occurred to very few to doubt this plausible explanation; very few thought of the peculiarly neurasthenic element in most of these affections, and very few indeed considered the enormous influence of external, moral, intellectual and other nervous stimuli upon the glands of internal secretion, and the secondary effect of these upon salivary, gastric, hepatic, pancreatic and intestinal mucous secretion, which, in its turn, was capable to produce with gross complications, as for instance, appendicitis, gastric ulcer, biliary disorders, etc. You all have seen patients who, to be cured of a chronic disorder, have successively submitted to a long series of mutilating operations, or such that have upset the normal anatomical relations of the hollow viscera. Each operation—as long as the patient observed the strict diet enforced during convalescence—reported a cure or at least an improvement, which, however, soon proved to be evanescent. The paper, dealing with the real pathology of the appendix in digestive troubles was very enlightening, and ought to be studied by all surgeons. Our secretary has done an excellent piece of work based on strictly scientific observation, and clarified by scientific criteria. It strengthened my conviction that certain hazy, loosely drawn conclusions of some of my colleages (*post hoc, propter hoc*) are untenable. Not only surgeons, but medical men also, do too often prefer this easy way of evading the necessity of explaining a difficult and obscure matter. I recall the subject of much controversy indulged in forty years ago by New York medical men, when a well known psychiatrist pretended to cure all forms of epilepsy by the use of the trephine. And it turned out to be a well observed fact, that after craniotomy,

temporary cessation of seizures is not rare at all. It happened that Dr. Henry B. Lands, then a leading surgeon, was asked by this specialist to trephine one of the latter's patients. Lands refused. Thereupon the specialist proceeded to operate himself and the patient's attacks, formerly very frequent, stopped for a time altogether. An indiscreet assistant, however, spoiled the game by telling that the operator in this case contented himself with a plain crucial incision of the scalp, which was afterward sutured. The cranium was left intact. So this revealed the interesting fact that a simple cutaneous incision had the same effect upon epilepsy as a trephining, as long as the patient believed in his doctor. Similar is, in my opinion, the effect of some of any operation upon certain functional disorders of the digestory tract. Disturbances of the central nervous system, leading to anomalies of internal secretion, these in their secondary consequences, producing chemical, bacterial and finally anatomical changes of a gross character, present a rational sequence of physiological anomalies. Dr. Kaufmann's paper has admirably exposed this view. As to the views on the so-called "Chronic intestinal stasis," upheld by certain surgeons, I will say, that in this condition constipation and gross changes in the nature of the affected viscera are the end product of a long series of secretory disorders. Stagnation of feces, ulcerations of the mucous membranes, etc., are not the cause of the deplorable state of these patients; the neurasthenia is not a sequel, it is the cause of all the trouble. How should an excision of the colon do more than f. i. eliminate ulcers and their immediate symptoms? How can such a heroic procedure cure a vicious state of the central nervous system?

Dr. R. Walter Mills, St. Louis, Mo.: I feel that it is a duty which is also a pleasure, to earnestly endorse Dr. Pfahler's statements regarding the X-ray diagnosis of chronic appendicitis. I might make possibly one slight exception. That exception has to do with ileostasis. There are certain cases that show what we judge to be ileostasis on X-ray examination that might be of appendiceal origin. There are also cases in which there is no evidence that the condition has anything to do with appendicitis, but simply the result of an atonic condition of the muscles of the ileo-cecal sphincter which is a common peculiarity of visceral tonus in that subject throughout. It would require extensive observations to definitely determine whether ileo-stasis is predominant in appendicitis. Otherwise, I must unreservedly second Dr. Pfahler's statements, especially regarding the fact that tenderness in appendicitis is intrinsically in the appendix, and I might add that in the majority of cases, it is intrinsically in the base of the appendix. Why, I do not know, unless it is because the base of the appendix is anatomically more fixed and consequently pain is more readily elicitated there on manipulation. I should like to ask the doctor what percentage of his cases show tenderness in the appendix. In my cases it is very large. This brings up another thought. It almost seems that through the X-ray we are obtaining

so large a percentage of tender appendices that one wonders whether the appendix may not be inherently sensitive in the same way that the kidneys are sensitive to pressure, or possibly we are getting evidence of what the pathologists are teaching that practically all appendices show inflammatory changes. This brings out another point: that it is not the essential tenderness alone but the degree of tenderness, taking into consideration the psychical condition of the patient, that is important.

There is another way in which the X-ray gives help in appendicitis, and that is in the study of the topography of the appendix. The whole question of habitus here comes in. The cecum is high in the sthenic, and lower in the asthenic and so on. It is helpful for the surgeon to know in advance that the appendix is retrocecal or in any other unusual position. I have tried to develop a method by which orthodiagraphic tracings are reduced and sent to the operating room, showing abdominal topography in each case. We are working on a method of suspending a camera to the ceiling and photographing the patient and the tracing at the same time for this purpose. There are technical difficulties to overcome, one especially is that pencil marks on the tracing glass throw a shadow on the body of the patient. This fault will probably be overcome by using multiple lighting.

In such cases as Dr. Pfahler recounted in which the appendix is high, very confusing symptoms arise. Again in those cases in which the inflamed appendix tip lies in the neighborhood of the rectum very atypical symptoms result. Dr. Pfahler, as I understand it, attributes such to the irritation offered by the distended rectum. I have had several such cases where there was an extensive secondary inflammation involving the rectum and pelvic colon, and inhibiting peristalsis and resulting in a picture suggesting cancer of the rectum.

Dr. John Bryant, Boston, Mass.: I have been studying this question of chronic invalids for seven years, trying to find out something about it. There are one or two points that I should like to mention. In the first place, it is pretty well established that there is a reflex between the pylorus and the ileo cecal sphincter. This was recognized one hundred years ago, and an article was written concerning it by MacEwen of Edinburgh in 1892. He made observations through a fistula, putting a tube into the ascending colon, and then noting the fecal material going through the sphincter.

Another viewpoint was not mentioned in this connection. The discussion seemed to boil down into the question, When is an appendix an appendix? The chronic form, I do not believe, is an appendix. In the so-called herbivorous type of individuals, the appendix reaches a further developmental differentiation than in the thin type of human. In this herbiverous type, we may have a long appendix, but there is a narrow base to it. In the course of fetal development, the base is more nearly pinched off. In both types early in the life of the fetus you have an appendix coming out from a conical base. In the asthenic

type, it still goes out conically, and appendicitis, if present, is usually chronic. In the herbivorous type, it is simple to get an infection bottled up in the appendix, and that is the type in which you get the acute process-appendices. In the other or conical carnivorous type, we get a recurrence of pain, but not suppuration and death. That point is useful in differential diagnosis. One night, I was on duty at the hospital, two appendices came in within an hour. On the basis of this type classification, I said that the first was a perforated appendix, which it proved to be. In the second case, the patient was apparently just as sick, but I concluded that it was one of those conical chronic appendices; I was right. The surgical people were wrong both times.

It is too late to go into a lot of these things that I should like to mention, but I wish to say that I have used a good deal of atropin. It relieves the spasms, resulting in the chronically distended painful cecum. The cecum is distended with gas, and if you can produce internal rest in the gut, you cut down the amount of gas, and go a long way towards curing the patient by relieving him from the pain of which he complains. I had a patient from Philadelphia, who was operated on there more than once for R. L. Q. pain, but the lady still had pain in the right lower abdomen. She was relieved of pain by medical treatment. I believe that the appendix is not the commonest cause of trouble in the large intestine. I think that you will find the bulk of the trouble to be actually in the hepatic flexure region, but often secondarily in the cecum and ascending colon.

Dr. Jacob Kaufmann, New York City: I think that Dr. Smithies pointed out an important fact. We want to distinguish between acute attacks and chronic appendicitis. I have made it a rule to have the appendix removed when I can elicit the history of an acute attack. Maybe you have to go back to childhood to get such a history as Dr. Brown pointed out. I have such an appendix removed as a prophylactic measure to prevent recurrence of further acute attacks. To remove an appendix for the purpose of curing chronic disturbances of the intestines—leave alone peptic ulcer or go so far as Dr. Draper indicated, to influence epilepsy. I do not hesitate to declare that it is absolutely useless, according to my experience and, as I understood Dr. Brown, according to his experience. There is hardly a day I do not see a patient whose appendix has been removed to eliminate chronic intestinal disturbances, with no effect achieved. The mistake is in thinking the chronic appendicitis the primary disease, when it is really secondary. The question is, What is its cause? As Dr. Smithies says, it is, as a rule, a part of a general pathological process of the colon, which may be acutely aggravated, and if you go back further and try to find the cause of that, you have to do as I did this morning with the cause of peptic ulcer. Try to find the cause of the functional disturbance of the gut. Those brought on by general disorders lead to constipation and infection, which bring on all these conditions which Dr. Smithies has described so well. After the appendix

is removed, these disorders will go on, unless we deal with the patient in a general way.

Dr. Frank Smithies, Chicago, Ill.: I do not wish to take up a great deal of your time, but perhaps some of you may remember that last year, before this Association, I mentioned the fact that in our cases of colon stasis in colons that had been resected, we found evidences of actual infection of the bowel itself. In many of these instances of stasis, the stasis seemed related to generalized low-grade infection of the bowel wall itself; very frequently we could find all the evidences of destruction and repair when the intestine was removed. It seemed that this damage to the colon very often was responsible for interference with the proper motor function of the intestine and was primarily responsible for the stasis. With respect chronic appendicitis, it is my opinion that frequently the chronic inflammatory lesions in the appendix represent nothing further than local infection of the same type which exists diffusely in the entire colon. It therefore follows that removal of the appendix, without the removal of the entire colon, can not make the patients well. Similarly such inflammatory lesions also exist in the gall bladder. To the surgeon examining this type of gall bladder, there appears little that is grossly pathologic, yet it is this type of gall bladder that gives us the highest per cent. of positive cultures. After operations upon appendix or gall bladder the patient's intestinal canal is placed in the ideal shape for healing. It is at rest and empty. Therefore, healing may take place and symptoms be absent for some time. In many cases, however, the colon wall infection again becomes active. Hence, we often hear people say, "If I had not had my appendix out, I should be sure that I was getting another attack of appendicitis."

Now some medicines seem to help. In the old days, when we gave large doses of salol, we supplied an anti-rheumatic type of medicine, a salicylate, which as all know is effective against "rheumatoid" coccus infections whether these be in the bowel wall or elsewhere. So those who formerly treated so-called "rheumatism of the bowel" with salicylates and then tell of the benefits of such treatment were perhaps not on the wrong track.

TERMINAL APPENDICITIS.

A Study in Indisposition, Inefficiency and Invalidism.

By John W. Draper, New York.

Except for the confusion and misunderstanding as to the physiologic pathology and symptomatology of appendicitis particularly as regards its chronic and terminal manifestations, it would be unnecessary to reiterate what has already been well said. To the French as foremost contributions in creative evolution, we owe the first word uttered more than a century ago regarding appendicitis. For more than three decades Fitch, McBurney, Murphy, Pilcher, Keen, Moynihan, Mayo, Deaver and a host of others fought for and taught the cardinal prniciples which constituted the truth about appendicitis, as they knew it. Without as broad a knowledge as we today possess, with a far keener vision than has been given most of us, they stood united for the fundamental principle of operating "when the diagnosis was made." Whatever the future may hold out in preventive medicine, the day which is sure to come, of preventing appendicitis by medical measures, has not yet dawned, and the present must remain in incalculable debt to the men of the past who by teaching early operation saved and will continue to save countless thousands of human lives. These great students of the inner abdomen whose daily task it was to observe all the symptoms in fullest detail, and then if indicated to open the abdomen and check and correct their diagnoses by actual findings, were the real internists of progressive medicine.

With this tribute to those whose work we have to carry on, let us consider in some detail how our problems differ from theirs. We have simply climbed the mast and broadened the horizon and with it the responsibilities. Briefly, they worked in a pus era; we in a clean; theirs was pathologic surgery, ours, at least in part, physiologic. Their chief job was, if possible, to save the patient from immediate death; ours to forestall the acute seizure and to prevent the development of those chronic protective symptoms of appendicitis called "dyspepsia," "indigestion," and "stomach trouble" by the laity; hyperchlorhydria, vagotonia and other

Latin names by the profession. These symptoms as well as the hepatic, pancreatic, duodenal and seco-colonic infectious histologic lesions, which we have come to recognize as the frequent underlying cause of such functional disturbances, may properly in a broad sense be called terminal appendicitis.

In communities where advanced medical thought prevails the ordinary acute attacks of appendicitis are, of course, becoming proportionately rare as the prodromal symptoms of so-called biliousness and so-called stomach trouble are more and more generally recognized to be appendicular in origin and to be treated surgically. This is an example of the preventive medicine of the future. It may be said then that every acute case of appendicitis is an odium upon the profession at large, for it is certain to have given symptoms which have been either overlooked or else erroneously treated often for years as hyperchlorhydria, vagotonia and other functional troubles. Indisputably it is far easier to follow the course of least resistance by advising operative delay; it requires the highest courage to urge surgical intervention. Those who favor long delay and medical treatment have the easy end of it—if a patient perishes because of delay, either by acute attack or because of terminal appendicitis become inoperable, the laity considers it the will of God. If, however, the surgeon striving to forestall such disasters loses a case, it is said on every hand that he is a rash enthusiast. So some of us travel the smug path of least resistance unmindful of opportunity and regardless of the increased responsibilities to the public placed upon us by the rapid march of events. We cannot ethically treat today as our fathers treated yesterday. It has been well said that the post-operative deaths which occur after we have been obliged to operate upon individuals exhausted by long and useless medical treatment should be charged direct to the medical attendant who denied to the patient early operation. Unless we put this mortality where it properly belongs, an enlightened laity will soon do so. The time is at hand then when acute appendicitis will become as rare as are the immense ovarian cysts and uterine fibroids, so frequently seen twenty years ago.

The point beyond this prevention of acute attacks to the prevention of colitis, cecitis, ileo-jejunitis, duodenitis, gastritis, pancreatitis and hepato-cystitis is our present goal. For continued observation of the inner abdomen proves that the appendix

stands in very frequent causative relation to gastric and duodenal ulcer, biliary and ceco-colonic disease, as well as to the less understood infections of the small gut. We stand squarely upon the principle that an appendix once diseased is always diseased. That until removed by operation it constitutes a double menace, first of acute inflammation, with or without gangrene and a 12 per cent. forced operative risk; or of terminal appendicitis with chronic dyspepsia, bilious attacks, hemicrania, mental derangement and lifelong indisposition, inefficiency and semi-invalidism.

It is well to forestall certain questions by answering them. How often has it been queried why many chronic intestinal invalids, well so named by Bryant, have so frequently had their appendices removed without the slightest improvement. Another insidious query; a sort of propaganda of non-resistance to disease is voiced when we are asked if there are not many cases of appendicitis recorded as cured by starvation, freezing and opium. Or again the doubtful and hesitant inquire whether one can be sufficiently sure of diagnosis as to justify operation.

If a careful examination is made of every case of unsuccessful appendectomy where the last state of the patient is often worse than the first, one of two conditions will almost invariably present—either the incision was of the discarded one-and-a-half-inch button hole type so popular in the last decade and through which no observations whatever could be made, or frequently the operation had been delayed too long so that localized peritonitis necessitated prolonged drainage followed by obstructive adhesions. Through a man's sized incision, which heals just as well as a button-hole, the best of us find it difficult enough to discern all the abnormalities, both congenital and acquired, in the belly of the typical intestinal invalid. How many of these unsuspected lesions are found and corrected, either in whole or in part, is known only to those who do this work day after day, and every busy surgeon will confess that not a week passes without his finding in the abdomen an unsuspected lesion often more serious than the appendix itself, and the correction of which would have escaped him except for careful and prolonged search. This in itself is the very strongest possible argument in favor of operating when the appendix is quiescent because extensive abdominal investigation is impossible in the presence of acute involvement. Obviously it is impossible for anyone to foretell precisely what

may be found in the human belly in addition to the lesion diagnosed. It is important to recognize that the atypical foetal development which undoubtedly favors adolescent appendicular degeneration also leads to other atypical arrangements unfavorable to human health. Lynch* and others have given intensive study to the important relation of embryology to gastro-intestinal disorders and I cannot urge its value too persistently. It, together with Rosenow's proof of specificity, afford our greatest aids in unentangling the mass of difficult and perplexing problems associated with chronic appendicitis. Embryology naturally broadens the field of gastro-enterology to embrace the pancreas and the liver, and prevents any surprise at the relation, for instance, of gall-bladder disease to appendicitis. Morphologically remote, embryologically they are one. It is logical that gall-stones or pancreatitis are frequently the terminal results of an early appendicitis which unrecognized until too late, had started the lesions which continued in spite of removal of the appendix. Failure of simple appendectomy then is very frequent and is to be looked for in part because of post-operative bands or more often because of the operator's failure to recognize either the frequent embryologic abnormalities or the specific infectious ulcers, etc., which we call terminal appendicitis.

What of the query regarding starvation, freezing, morphine, and diet as a cure? Two factors, tortion and occlusion determine the pathology of the appendix to be either gangrenous or purulent. So long ago that we should blush to record it, Murphy, clear-headed student and teacher, proved and taught that pus under pressure had a very different coefficient from free pus. And this, long before we knew anything of bacterial specificity. What possible effect can rest and ice have upon tortion and occlusion save to benumb that greatest of protective symptoms, pain, and to destroy its diagnostic value. What possible form of medication can be imagined, save by the self-hypnotist which can release the cicatricial stenosis of a tube which is already closed at one end. Until the biologists discover for us a selective fibrolysin this stenosis will stand as a menace until removed by the admittedly crude method of operation.

Others ask as to diagnosis. Our simple rule being to operate

*Lynch, J. M., Diseases of the Rectum and Colon, Chapter 4, 1914. Lea & Febiger.

when the diagnosis is made, its establishment is of vital importance. The modern differential diagnosis of chronic appendicitis is based upon the simple and most pertinent truth that every subjective symptom is protective and purposeful. This can easily be explained by its relation to the sympathetic system. Progress will be delayed until it is generally understood that even loss of weight is distinctly protective.

Protective or Esoteric Symptoms of Alimentary Canal.

Lynch and I* have repeatedly referred to this and no more scholarly exposition of the subject exists than that by Drake.** Except in 10 per cent. of cases in most of which the pathology is that of ulcer or cancer "sick stomach" are sound. Every stomach symptom is esoteric and more than half primarily from the appendix. Back of the vomiting; back of the nausea; back of the gas, the heart burn and the bloating, is a cause. That these symptoms can be modified by diet, hygiene and drugs does not in the least alter this fact. It simply clouds the issue. In our personal experience Lynch and I have found it necessary to differentiate the following conditions from appendicitis. Acute hydronephrosis; stone in kidney and ureter, psoas spasm, mobile cecum, elbow deformity, tuberculosis, both hyperplastic and diffuse, gall-stones, cholecystitis, ulcer of stomach and duodenum, mesenteric cyst, strangulated ovarian cyst, acute pancreatitis, acute nephritis.

There are four well-known diagnostic methods in general use. In order of importance and reliability they are: History, X-ray, physical examination and lastly chemical examination of stomach and duodenal contents. It is a very interesting chronicle of progress that in the experience of many of us the X-ray has moved from the fourth to the second place in this list. This is wholly because we have learned to utilize it to interpret the functional conditions, delay, etc., rather than as was formally the case to depend upon the mere morphological findings relatively so unimportant. What earthly difference does it make whether a stomach is largely in the pelvis so long as it empties, for Bryant has taught us that some of them belong there. Many ingenious efforts to stabilize and to accurately interpret the

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**A new development in sanatorium treatment.

chemical findings as indicators of diseased condition in the stomach and duodenum have been made, but in spite of this their diagnostic value most unfortunately has slowly but surely sunk to the fourth place. And in the opinion of many it's a very distant fourth. This is by no means true of the fractional method of Dreyfuss, which promises to give most valuable information as to bacterial infection of stomach and duodenal walls. And this is perfectly logical if considered in line with the accepted fact that, aside from the above mentioned infections, 90 per cent. of all stomach complaints are simply functional and represent protective efforts of the organism to heal a lesion remote from the stomach. In chemically examining stomach and duodenal contents, therefore, we are usually seeking for a needle in a haystack, the true cause of the protean changes in acidity and other chemical components except in cases of actual wall infections often being twenty feet distant from the stomach; often in our experience a cancer of the rectum: usually an appendix. Who could expect constancy under such conditions, and why not accept Smithies' scholarly conclusions as to the unreliability of the chemical findings. He knows.

The phase of terminal appendicitis to which we have recently given particular attention is cecitis. In our paper upon Segmental Infections of the Colon we have discussed the fundamental infections and the peculiar focal arrangement of this acute form and its direct causative relation to the appendix. Its treatment is by ileostomy and by this technique, which we owe to Lynch who performed the first one in this country independent of one done previously by a French surgeon, and by it alone, can these lesions be cured. Cecitis, also in close etiologic relation to the appendix, is wholly different. Its origin is complex, being due also in part to the partial obstruction so frequently found in these cases at the hepatic flexure and which we have called elbow deformity. While in early life appendectomy and cecal plication may be depended upon usually to prevent cecitis nothing short of the extensive resection which we have called developmental reconstruction will cure when once the disease is firmly established.

To the list of 29 cases of developmental reconstruction of the colon reported last year by Lynch and myself, we add six. One of these, an extensive resection for tuberculosis and already in

extremis (see figure), died a month after operation—a death not properly chargeable to surgery but to the doctors who withheld operation until too late. This mortality rate has been two in 26, or 7.7 per cent. Probably this can be reduced somewhat by continued experience and improved technique, but the operation will, of course, always remain a formidable one. Without exception the improvement reported in the previous paper has been so constant as to justify us in concluding that in carefully chosen cases developmental reconstruction of the bowel is not only justifiable but offers the only means of curing a rather large group of chronic intestinal invalids. McFarland's study of the pigment occurring in the attenuated and atypical ceco-colonic walls of our patients has been published and we agree with his deductions. This has been found in another of our cases by another pathologist, Sondern, whose findings as to distribution of the pigment, agreed with McFarland's. Now we feel sure that in addition to the pigment which can often be detected by the naked eye, another valuable indication for colonic reconstruction is the presence of extensive mesenteric glands. These we have also frequently noted in epileptics; an observation which we consider of great importance. We cannot emphasize too greatly or reiterate too often the diagnostic value of Lynch's elbow deformity at the hepatic flexure. It can usually be found by proper X-ray study. This mechanical narrowing of the colon often causes amazing dilatation of the cecum as shown in the accompanying sketch and this is particularly true when rotation has been atypical and when fusion and delamination have been incomplete. Barber has shown the effect of obstruction here to be duodenal dilatation. This begets partial obstruction and there follows that peculiar syndrome of symptoms modified in degree but resembling those of total duodenal obstruction described by me fifteen years ago. These are not directly of bacterial origin, but a bacterial element is introduced by the colonic segment.

Some very important considerations of relationship between mental derangement and local foci have been considered during the past year. No one can practice gastro-intestinal surgery without being struck by it. The most notable paper of which I have knowledge is one by Henry Cotton, Director of the New Jersey State Hospital for the Insane, read before the New York Psychiatric Society in April. Until today the psychiatrist was a

creature quite apart from the ordinary doctor or surgeon, and Cotton shows how we are all getting together on a common ground. After presenting statistics which showed that much insanity is merely a terminal symptom of toxemia, he urged that psychiatry was no longer a matter of psychoanalysis by which it was sought to trace our mental and moral shortcomings to irregularities in the sexual lives of our Nordic, Alpine, Mediterranean and other prehistoric ancestors, but rather an up-to-date search for the physical basis of the trouble—often a local bacterial focus. Many were in the teeth and tonsils, others were abdominal, often appendicular. What had proved true of paresis as regards our ability to cure it he hoped to find true of many manic-depressive states, and his statistics surely justified his hopes. In this connection I report herewith the history of one chronic epileptic whose colon was developmentally reconstructed by us June 8, 1917. Although she had had frequent attacks for the preceding three years, the intensity and frequency having increased prior to operation, with the removal of the infectious area, consequent upon the reconstruction she has been free from attacks since operation. This case has been seen by Drs. Cotton and Satterlee. I also present the statistical records of the hemicranial headaches of the case referred to by me last year at the meeting of this society and am glad to say that this woman has remained entirely free from headache, has been restored to a normal mixed diet and has found herself able to carry on an immense amount of Red Cross work during the past year. Prior to the operation she was a human derelict, contemplating suicide. We hold no brief for the operation save that as to results we believe; as to explanation and interpretation we remain agnostic. In connection with Dr. Cotton's work it is also pertinent to report an X-ray comparative study of father and son in manic-depressive insanity. It is planned to operate upon the father this summer and I shall hope to present the results before you next year.

Surely the gastro-enterologists are not to fall behind the introspective psychiatrists in recognizing that there is a physical basis for most human ailments and that whoever would help best must seek to find and eliminate it.

DISCUSSIONS.

Dr. John W. Draper, New York City: With regard to my reference to epilepsy, I wish to continue in a state of humility, despite

Dr. Brown's statement as to our exalted position, and say that we have ventured to operate on one case only. That was in a woman, who had been shown by very careful medical study to have a delay of about one hundred and twenty-five hours on her right side; and a number of very capable gastroenterologists had endeavored to lessen that delay. Failing in this, they had asked us to do this operation of right-sided resection, called by us developmental reconstruction of the colon. I must say that, to our great surprise, she has remained better ever since the operation. She is a very intelligent woman. She is still under our care, and I intend to report the case next year, if I can, and state what progress she makes.

Regarding the endocrine system, somebody asked about the leaking sphincters. We have found out of ten leaking sphincters that we have studied, that seven could be closed by giving 10 mm. of epinephrin immediately. Leakage is of course merely a symptom.

Dr. White asked for an expression of opinion as regards cecostomy. Beyond ordinary indications for a stoma in this region it is never indicated if the appendix is available. It depends upon the type of infection. It is all right to do cecostomy in case of certain mild infections, but many extend into the secum, and cecostomy is then undesirable. We, therefore, do an ileostomy. We have twenty of these cases, and they are interesting from their physiological standpoint. They have generally improved in a way that has astonished us, because it is contrary to what we have been taught by the physiologist. These cases are reported in our paper on Colonic Infections. We have several patients who have had permanent ileostomy for some years. One is Dr. Lyon of New Haven, who was at the meeting last year. That operation was done to reduce papillomata. The patient is perfectly satisfied with the result. He can walk for miles, and does not wish to have any change made. I think that we owe a great deal to Dr. Lynch who devised this operation and practised it first in this country. It gives immediate relief, and is relatively free from danger.

I wish to thank Dr. Brown for calling attention to a statement that I made, that the stomach does not seem, in many of these conditions, to be involved. It is true that the operating surgeon cannot see the interior of the stomach, and I have no doubt that there are many lesions which we do not see; notably, infections of the alimentary canal wall and in proof of Dr. Brown's statement and my acceptance of it, I would say that we have been much amazed by the improvement in several cases of chronic intestinal invalids from whom we have removed an appendix and found no microscopic or gross lesion in it, and yet having followed these cases for years, and found them cured we have concluded that the symptoms were caused by traction upon a short mesentery.

THE FRACTIONAL STUDY OF THE GASTRIC CONTENTS.

By G. W. McCaskey, M. D.,
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The Ewald test breakfast, removed in one hour, has been one of the most useful and widely used of all conventional clinical methods. It forms the basis of most of the literature on gastric secretion studied from the clinical side. As a basis of comparison, it has been invaluable because of its uniformity and almost universality in different languages and countries. Its objections and limitations have, however, always been apparent to every thinking clinician. For instance, its removal in one hour was based upon the assumption that the flood of acid secretion would reach its crest at that time, and perhaps coincidentally with this, the most conspicuous factor of gastric secretion, the maximum output of other constituents as well. Such a uniformity of secretory phenomena would, of course, be entirely anomalous and, in fact, does not occur.

The curve of acid secretion, as shown by Rehfuss, Best and others, is quite variable. For many years I have been impressed and confused by the bizarre findings of analyses of the Ewald test meal. Without any probable change in pathology and with none in symptomatology, the same patient, with precisely the same technique, will give utterly discordant results on different occasions closely related in time. I have more than once seen a very low hypo-acidity change to a relatively high acidity and vice versa within a few days. Such fluctuations are probably more often due to time variations in the rate of secretion rather than to actual changes in maximal acidities. The crest of the secretory wave, in other words, may occur in thirty or forty minutes in some instances and in considerably more than an hour in others. These results are modified by various factors, such as motility, rate of secretion, character and quantity of meal, possibly vasomotor or muscular tonus, etc. Various modifications of the Ewald meal, such as the Leube-Riegel meal, have, of course, overcome some of these objections, but with any kind of a meal,

large or small, the difference between the chemical findings at any one moment and the chemical curve over a considerable period of time may be compared to the differential value of a Roentgenogram of a stomach containing a barium meal, which records the picture in the fraction of a second, and a Fluoroscopic observation of a series of peristaltic waves in the same stomach over a relatively long period of time. As a matter of fact, the values of the latter are obviously so much greater that it is a question of contrast rather than comparison. The absurdity of basing a clinical conclusion upon the chemical findings in the gastric contents at any fixed or invariable period of time following the ingestion of any kind of a meal is too obvious to require comment. It may still be necessary to meet the exigencies of clinical problems by the same technique, but it should at least be done with a clear apprehension of its sharp limitations and glaring uncertainties.

The purpose of this brief communication is to emphasize the unreliability of the conventional methods and call attention to the fractional methods above referred to, which give information of much greater value. The difficulties and objections to the repeated introduction of the ordinary stomach tube at sufficiently frequent intervals and for a sufficient length of time to give us the desired information are insurmountable excepting in very rare instances in which the patient's tolerance of such procedures is quite remarkable, to say nothing of the burden which the repeated introduction of the tube imposes upon the clinician or his assistant. The introduction of the capillary tube by Einhorn, while originally designed for the study of the duodenal contents, paved the way for a more continuous study of gastric secretion which was later carried out by Rehfuss with very interesting results. For stomach work I use both the Einhorn and Rehfuss bulb, but consider that latter somewhat preferable because of its larger apertures permitting the passage of digested material which would not pass through the finer perforations in the Einhorn bulb. On the other hand, this very fact sometimes permits the blocking of the tube by coarser particles which would not enter through the Einhorn bulb.

The bulb attached to the capillary tube is simply swallowed by the patient with a little food or fluid and is carried down into the stomach by repeated acts of deglutition. In the large majority

of cases this is done without difficulty by the patient. The protruding end of the tube can be conveniently closed by a stop cock, which can be opened when specimens are desired and closed at other times to prevent leakage. It is only necessary to open the stop cock and insert a 5 or 10 cc, syringe and remove a small quantity, say 1 to 3 cc. for analysis. This takes but a moment of time and does not cause the slightest annoyance to the patient, who would not necessarily awaken if asleep. In fact, I have actually had nurses remove many such specimens when patients were asleep without awakening them. I commonly have the specimens taken at fifteen-minute intervals, beginning twenty or thirty minutes after taking the Ewald test meal and extending over a period of from one to two hours, or until the chemical analyses, which are immediately made as the specimens are secured, indicate that the active phase of secretion has ended. While this is commonly limited to the titration of free and total acidities, any other phase of gastric secretion, such, *e. g.*, as proteolysis, could be equally well studied. A protruding portion of the small capillary tube is placed at one angle of the mouth and the other extremity attached to the clothing by a safety pin or to a light rubber band around the lobe of one ear. Most patients become accustomed to this tube and can tolerate it indefinitely. It is often kept in situ for days or even weeks, either in the stomach for the purposes indicated in this paper, or allowed to pass through into the duodenum for the purpose of studying the duodenal secretion. In one of my cases of gastro-duodenal ulcer, which was proven by the operation to be on the duodenal side of the pyloric gate, the patient was fed by one tube, the bulb of which was well down in the duodenum, while through another, the bulb of which remained in the stomach, the excessive secretion of acid was removed and alkalies introduced to neutralize the residual acid. This sort of procedure was kept up for about two weeks, both procedures being repeated at frequent intervals day and night without disturbing the patient to any degree.

While my own clinical observations in the fractional study of gastric contents has been mostly limited to the Ewald test meal, there is no reason why it should not be utilized with the Leube-Riegel or any other larger meal, the observation extending over a sufficiently long period of time.

Now and then certain technical difficulties are encountered. For instance, the bulb for some reason fails for a time to find its way into the fluid contents of the stomach, in which event, of course, no specimen can be obtained. This does not usually last long nor does it occur often. Slightly withdrawing the tube, a few repeated acts of deglutition or forcing a little air into the stomach with a Luer syringe will overcome the difficulty.

Now, as to the clinical interpretation of these observations; it is not my intention at present to do more than record my general impressions with a reference to a few cases. There are certain fundamental physiological phenomena which must be taken into account in this connection. There seems to be considerable difference of opinion as to what really constitutes a normal acidity and certainly as to the time in a given type of meal when the crest of the acid secretion will be reached. Boldyreff's conclusion that gastric secretion is quite constant at .5 per cent. HCl, being modified by a combination with food, etc., seems entirely incompatible with clinical observations such as those above referred to. Rehfuss well says that the height of secretion is in many instances reached in one hour, but certainly not in all. As illustrating one group of cases to which I have referred, it might show a hypochlorhydria and not an achlorhydria at the conventional one hour period.

One patient, a man of forty-eight, with latent lues, showed a complete absence of free HCl in exactly one hour, while in subsequent periods up to two hours and forty-five minutes free HCl was present in from 25 to 52 degrees, the highest acidity being reached in two hours and ten minutes. This patient had no definite or important stomach lesion and made a complete recovery under specific and suitable hygienic treatment.

Another patient, a man age thirty-two, showed no free acidity at forty minutes, 20 degrees at one hour, while in one hour and fifty-five minutes the free HCl had risen to 80 degrees. These are simply illustrative cases from a larger group, which is certainly not rare.

It is my intention in a future communication to enter into a more detailed study of these cases and the clinical problems involved, but if I have sufficiently emphasized and illustrated the two main points mentioned at the outset I have accomplished all that I have intended at this time.

FURTHER EXPERIENCES WITH THE DIRECT EXAMINATION OF THE DUODENAL CONTENTS IN AFFECTIONS OF THE GALL BLADDER AND ALLIED ORGANS.

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The direct examination of the duodenal contents (bile and pancreatic secretions) in affections of the liver, gall bladder and pancreas is so self-evident that it hardly appears necessary to discuss its advisability. The fluids of all accessible cavities are eagerly studied (gastric contents, faeces, urine, blood, spinal fluid) and their characteristics found useful in establishing a diagnosis. Why should not this be done with the duodenal contents? The latter, as it is well known, carry with them secretions and excretions of vital import for the existence of the organism (duodenal and pancreatic juices and bile). It is but natural that affections of the liver, gall bladder and pancreas will gain considerably in clearness by frequent and thorough explorations of the duodenal contents.

In two previous papers I* ** have published the results of my findings in this respect. In the present article I intend to report my new experiences with the direct examination of the duodenal contents in affections of the gall bladder and allied organs. For the sake of brevity I shall describe all the cases in which the direct examination of the duodenal contents was of material aid in diagnosis in the subjoined table, while a few of them will be sketched in greater detail. The latter are as follows:

Case I (table number 11).—Gastric Ulcer and Cholecystitis, February 2nd, 1918. Mrs. J. T. P. had a sudden attack of pains in the epigastrium and slight jaundice, requiring morphine one and one-half years ago.

These attacks of gas and distress in the stomach occurred after

*Max Einhorn: Direct Examination of the Duodenal Contents as an Aid in the Diagnosis of Gall Bladder and Pancreatic Affection. *Amer. Jour. Med. Sciences*, October, 1914.

**Max Einhorn: The Duodenal Tube as a Factor in the Diagnosis and Treatment of Gall Bladder Disease. *J. A. M. A.*, June 19, 1915.

getting tired or overeating once a month, later oftener. Patient also suffered from constipation and slight pains relieved by bicarbonate of soda. On January 10th patient had a severe attack requiring a hypodermic lasting two days. Since then there was a temperature of 100-101 up to February 7th. Patient felt weak and lost 17 pounds in weight.

Present condition: Patient looks somewhat pale. There is nothing abnormal to be elicited in the chest organs. The stomach extends one to two fingers below the navel. The epigastrium is painful to pressure. The liver is not enlarged.

The gastric contents one hour after a test breakfast shows: HCl 1, acidity 65. Duodenal bucket (II-9-18) passes the pylorus and shows a blood stain at 41-42 cm., bile 55 cm. down to the end.

The examination of the duodenal contents fasting conditions shows as follows: Yellow, very turbid, alkalinity=40, A=20, S=7, T=4.5. The blood count is as follows: RBC=6,000,000; HB=100%. WBC=8,000, Polys=68%. The blood pressure is 128 mm. The urine does not show any albumin or sugar or bile. The temperature is: morning 99, evening 100.5. X-ray emanation by Dr. Stewart revealed a pathological gall bladder with adhesions and marked propyloric spasm.

The diagnosis was gastric ulcer and cholecystitis, probably due to gallstones. Patient was treated by duodenal alimentation and instillation into the duodenum every other day of 15 c.c. of either a one-half per cent. argyrol solution or a one per cent. ichthyol solution.

After a few days' treatment the temperature was normal, and the patient felt better. The duodenal contents began to look better (less turbid).

Case II.—Mrs. R. K., November 1, 1917. Cholelithiasis (table No. 6).

Patient was well until four years ago when she began to be troubled with pain in the stomach 2-3 hours after eating. These attacks would occur once or twice a month for several days and last one-half an hour. Six months later the condition became worse.

The attacks would occur more often and were more severe. The pains would appear 5-6 hours after eating and would spread over the entire stomach. Vomiting would bring relief. This condition became worse up to the present time, the patient having lost 40 pounds during the last six months.

Present condition: Two to three hours after eating patient complains of severe pain in the stomach. These pains continue until the stomach is emptied by vomiting, which is usually 4-6 hours after meals. The attack of vomiting lasts about 1-2 hours after which the patient is very weak and complains of muscular pains all over the body followed by chills. The latter condition lasts about one hour. The patient looks slightly icteric. The chest organs do not reveal anything abnormal. The stomach is slightly dilated extending to two fingers width below the navel. The liver is slightly swollen overlapping one finger's width the margin of the ribs in the right mammillary line.

The gastric contents revealed as follows: HCl=O:Acidity=30; no blood. The duodenal bucket was 65 cm. in length; bile 35-65 cm.; blood stain 49-51 cm. The duodenal contents on XI-117 fasting condition are yellowish brown, twice normal amount; alkalinity=20; A=10; S=4; T=6. On XI-5-17 the duodenal contents are yellowish green and turbid. A=10; S=.5; T=3. The blood count: RBC=3,200,000; HB=85%; WBC=8,000; Pols.=79%.

The diagnosis of gallstones was made and an operation recommended. Dr. Willy Meyer performed the operation. A number of hazel nut-sized stones were found in the gallbladder and two were discovered, lodged in the common duct. Cholecystectomy was done and the patient made a perfect recovery.

CASE III.—Mrs. K. S. Chronic pancreatitis and jaundice due to pressure on the common duct. October 1st, 1916. For the last five years the patient complained of severe diarrhea, epigastric distress, weakness and loss of weight. Patient looks pale and thin, tongue not coated. Chest organs are apparently normal. The stomach extends to about one finger's width below the navel (splashing sound). The liver is not enlarged.

The examination of the gastric contents one hour after a test breakfast shows as follows: HCl=O; Acidity=4; no rennet; very little fluid; pieces of poll not changed; no blood. The bead test revealed that the beads appeared in the stool after 42 hours, with fishbone, catgut, fat, meat and thymus containing nuclei, present.

On October 7th, the patient had pains in the right upper abdomen, felt chilly and became slightly jaundiced. The duodenal contents were examined on October 12th, 1916, in the fasting condition, with the following result: watery, no bile, alkalinity=10; A=2; S=1; T=trace.

The diagnosis of chronic pancreatitis and probably also gallstone colic was made. In view of the fever which was continuous and symptoms of cholangitis, an operation was recommended. On October 19, 1916, the patient was operated by Dr. Willy Meyer. No stones were found in the gallbladder; the pancreas was thickened and hardened; the glands in the neighborhood swollen. An appendectomy and cholecystostomy were performed. Patient made a good recovery. The bile running from the fistula examined on October 24th, 1916, showed: A=2; S=0; T=0; Alkalinity=40. The draining of the gallbladder was kept up for a number of weeks and had a remarkably good effect on the general condition of the patient. She has picked up in weight. Her diarrhea has disappeared and patient remained pretty well up to date (March, 1918).

CASE IV (table No. 20).—October, 1916. Mrs. R. Carcinoma of the stomach and pancreas.

The patient complained of gastric disturbances for about ten weeks before consulting me. The chief complaints were pains one hour after meals, loss of appetite and a loss of fourteen pounds in weight. The gastric contents showed: HCl+; Acidity—74; occult blood

present; no food retention. The string test showed a blood stain at nineteen inches from the lips and bile below 23 inches, showing permeability of the pylorus. A resistant mass was palpable below the left costal margin. Examination of the duodenal contents was as follows: Clear, yellow (golden); alkalinity=20; A=3; S=2; T=0. A diagnosis of carcinoma of the stomach (lesser curvature), probably involving the pancreas was made.

As the patient was quite young, about 38 years, an operation was decided upon, in order to attempt to bring relief if in any way feasible. The incision, however, showed a considerable malignant tumor of the lesser curvature of the stomach extending and involving the pancreas. The pylorus was free. The mass was left intact and the wound closed.

Two to three weeks after the operation the pains were excessive and the patient could not take the lightest food without suffering greatly. In order to bring some relief and help nutrition, duodenal alimentation was instituted. The food entering the duodenum not touching the stomach, thus leaving the tumor unmolested, proved to be a great boon to the patient. She rallied considerably and felt pretty well for a while. In resuming the ordinary way of alimentation the pains returned and opiates were constantly required to reduce the suffering and make the condition bearable. A few months later the patient asked for a new period of duodenal alimentation which was given her again with some benefit. The patient continued to live and to suffer until nothing was practically left of her body, excepting skin and bones and then she died.

In this case it was of special interest to watch the function of the pancreas which was frequently tested. We give here the different examinations which always showed an entire absence of the trypsin ferment. The examinations were as follows:

10-21-16. Alkalinity=20; A=3; S=2; T=0.
10-23-16. Alkalinity=5; A=3; S=2; T=0.
10-27-16. Alkalinity=30; A=4; S=5; T=0.
2-6-17. Alkalinity=30; A=0; S=trace; T=0.

Case V (table No. 22).—J. F. D. Duodenal ulcer with periduodenal abscess. January 13th, 1917. J. F. D., about forty-six years old, was troubled for a number of years with pains in the upper abdomen late after meals, covering a period of 4-6 weeks, intermingled with intervals of perfect euphoria lasting 6-8 months. For the last 4 weeks patient was suffering from a similar attack of pains in the abdomen. In addition to the old symptoms patient experienced great weakness and had off and on chilly sensations, accompanied by a slight rise of temperature.

Present Condition.—Face is flushed; tongue is coated; chest organs apparently normal. In the abdomen there is tenderness to pressure over the epigastric region. The liver dullness is increased upwards up to one finger below the right mammilla and downwards two fingers below the costal margin. At the lower margin of the liver a resistant

mass can be palpated three inches in length and one and one-half inches in thickness. The gastric contents showed HCl+; Acidity=74; no blood. The stool blood negative. The Wassermann was negative. The thread test showed a blood stain from 23-23½ inches, and bile below 24 inches. The duodenal contents were as follows: golden yellow, clear; alkalinity=20; A=8; S=3; T=3. The blood was RBC=5,300,000; HB=88%; WBC=13,760; Poly=79%. This examination was made on the I-23-17. On the I-24-17 the blood was: whites=14,000; Poly=80%. The temperature fluctuated between 99-102° F. and was of an irregular type. The X-ray examination did not show anything definite. The urine revealed the absence of albumin or sugar and the presence of urobiligon.

With regard to the diagnosis the past history and the thread test pointed to a duodenal ulcer. While the present symptoms and the swollen liver with the rise in temperature and the considerable leukocytosis seemed to indicate an infectious process probably due to some gallbladder disease. The clear golden yellow bile appeared to negative an infectious process in the gall ducts. The resistant mass beneath the liver and the temperature curve in conjunction with the leukocytosis pointed to a suppurative process in the upper abdomen near the liver requiring surgical aid. The operation performed by Dr. Willy Meyer disclosed a periduodenal abscess. The gallbladder was found to be normal. About 3-4 ounces of pus were evacuated and the wound drained. The temperature continued for a number of days. The patient being extremely weak and exhausted duodenal alimentation was instituted. Under this regime his strength increased from day to day and the fever disappeared. The patient then made a perfect recovery and regained in a few months the forty pounds he had previously lost.

In looking over the tables we find 18 cases of probable cholecystitis with turbid bile. In ten of these, in which the diagnosis pointed to gallstones, operations were performed. In eight stones were found, while in two (cases Mrs. T. K., No. 2, and Mrs. A. L. M., No. 8) no stones were found. In one case, however, the bile aspirated during the operation from the gall bladder looked dark brown and was turbid, representing exactly the sample, which had been previously obtained by duodenal alimentation. In this case the gall bladder was excised; the mucosa was found to be inflamed and thickened, representing the strawberry type. In a few of the eight non-operated cases (11-18) the X-ray report likewise seemed to indicate some pathological condition of the gall bladder. Cases 19 and 20 both representing severe pancreatic lesions, which came to operation, one benign the other malignant, have been described in detail. They are of

TABLE OF CASES IN WHICH THE EXAMINATION OF THE DUODENAL CONTENTS WAS OF DIAGNOSTIC AID (May, 1916; March, 1918).

Case.	Name.	Diagnosis.	Date.	Examination of Duodenal Contents.				Appearance of Duodenal Contents.	Remarks.
				Alkalinity.	Amylopsin. M. M.	Steapsin M. M.	Trypsin M. M.		
1	Mrs. B—	Cholecystitis and probably Cholelithiasis	5-24-16	10	6	0	3	Greyish, tinged with yellow (straw color) turbid, mucous.	Rennet +. At operation stone found in the common duct.
2	Mrs. L—	Cholelithiasis.	6-15-16	10	1½	0	½	Slightly turbid yellow, mucous.	Operation — gallstones found.
3	Mrs. T. K—	Cholecysitis	6-16-16	20	5	1	3	Yellow, turbid.	X-ray showed a circular shadow, due probably to gallstones.
			VI-19-16	30	8	2	3	Purple, clear.	Operation for adhesions over caecum; gallbladder contained no stones.
4	Mrs. B—	Cholelithiasis	III-2-17	—	8	Trace	0	Whitish, turbid trace of yellow.	Operation — gallstones found.
5	Mrs. B. H—	Cholelithiasis	IV-20-17	30	0	0	0	Yellow, turbid.	Milk unboiled=coagulated. Milk boiled=no coagulation.

TABLE OF CASES IN WHICH THE EXAMINATION OF THE DUODENAL CONTENTS WAS OF DIAGNOSTIC AID (May, 1916; March, 1918).—*Continued.*

Case.	Name.	Diagnosis.	Date.	Examination of Duodenal Contents.				Appearance of Duodenal Contents.	Remarks.
				Alkalinity.	Amylopsin. M. M.	Steapsin M. M.	Trypsin M. M.		
			IV-24-17	0	4	1	3	Yellow, clear.	Operated upon by Dr. Willy Meyer. Gallbladder enlarged, containing seropurulent fluid and stones. (Cholecystectomia).
6	Mrs. K—	Cholelithiasis	XI-1-17	20	10	4	6	[1]Yellowish, brown, twice normal am't.	Gallstones found at operation. Case to be described in detail.
			XI-5-17	—	10	0.5	3	[2]Yellow, green, turbid.	
7	Mrs. S—	Duodenal ulcer; Cholelithiasis	XI-9-17	30	10	4	6	Yellow, tinge of green, slightly turbid.	Operation — 200 stones found in gallbladder. Duodenal bucket test = blood at 22½ inches. On XI-18-17 rise in temperature and blood count= Polys. 78%. W. B. C.=10,200.

TABLE OF CASES IN WHICH THE EXAMINATION OF THE DUODENAL CONTENTS WAS OF DIAGNOSTIC AID (May, 1916; March, 1918).—*Continued.*

Case.	Name.	Diagnosis.	Date.	Examination of Duodenal Contents.				Appearance of Duodenal Contents.	Remarks.
				Alkalinity.	Amylopsin. M. M.	Steapsin M. M.	Trypsin M. M.		
8	Mrs. A. L. M.	Cholecystitis	X-11-17 X-13-17	(Gastric Contents HCl+Rc=40.) 20		8	2	3	Green, brown, turbid.	Operation: X-27-17; no stones found; gallbladder looked like velvet and dark brown; bile was dark brown, resembling Kumbocher beer. X-ray = Diagnosis of gallstones.
9	Mrs. J. H. Mc.	Cholelithiasis	XI-24-17	20	10	6	4	Dark green with a tinge of yellow and slightly turbid.	Operation: XI-26-17. Gallstones found in gallbladder and common duct. Blood count=R. B. C.=4,800,000. W. B. C.=11,000. Polys=82%. H. B.=90%. Temperature: 99-101° F.

TABLE OF CASES IN WHICH THE EXAMINATION OF THE DUODENAL CONTENTS WAS OF DIAGNOSTIC AID (May, 1916; March, 1918).—*Continued.*

Case.	Name.	Diagnosis.	Date.	Examination of Duodenal Contents.				Appearance of Duodenal Contents.	Remarks.
				Alkalinity.	Amylopsin. M. M.	Steapsin. M. M.	Trypsin M. M.		
10	Mrs. R. F—	Cholelithiasis	II-12-17	40	2	2	4	Whitish, no bile.	Operation, Stones found. Cholecystectomy.
11	Mrs. P—	Gastric Ulcer; Cholecystitis	II-8-18	40	20	7	4½		Case described in detail.
12	Mrs. I. N—	Peptic Ulcer; Cholecystitis	VI-17-16	30	5	0	½	Milky, cloudy, no bile.	X-ray = gallbladder disease. No operation.
13	Mrs. W. D—	Cholecystitis	VI-27-16	25	7	8	3	Watery, cloudy.	Blood Count=W. B. C.=12,000. Polys=71%.
14	Miss B—	Peptic Ulcer; Cholecystitis	X-3-16	30	2	0	0	Light, yellow, turbid.	No operation.
15	Mr. W. N—	Cholecystitis	III-2-17	30	7	2	5	Yellowish, slightly turbid.	No operation.
16	Mrs. P—	Cholecystitis	IV-17-17	0	2	1	0	Greyish, turbid.	X-ray=Visualization of gallbladder.
17	Mr. Z—	Gastroptosis; Cholecystitis	XI-10-17	10	3	5	5	Yellow, turbid.	X-ray=Ulcer of stomach.

TABLE OF CASES IN WHICH THE EXAMINATION OF THE DUODENAL CONTENTS WAS OF DIAGNOSTIC AID (May, 1916; March, 1918).—*Continued.*

Case.	Name.	Diagnosis.	Date.	Examination of Duodenal Contents.				Appearance of Duodenal Contents.	Remarks.
				Alkalinity.	Amylopsin. M. M.	Steapsin. M. M.	Trypsin M. M.		
18	Mrs. P—	Cholecystitis	XI-16-17	30	7	5	6	Yellowish, green, turbid.	X-ray = Probable distended gall-bladder. H. B. =70%; W. B. C. =11,400; Polys =79%; Wassermann 1+.
19	Mrs. K. S—	Chronic Pancreatitis; Jaundice due to pressure	X-12-16	10	2	1	Trace	Watery, no bile.	Case to be described in detail.
			X-24-16	40	2	0	0		
20	Mrs. R—	Carcinoma of Pancreas	X-21-16	20	3	2	0		
			X-23-16	5	3	2	0		
			X-27-16	30	4	5	0		Rennet absent.
			III-6-17	—	0	Trace	0		Liver enlarged;
21	M. H. W—	Carcinoma of Pancreas	IX-9-16	—	6	0	0	Whitish.	case described in detail.
22	Mr. D—	Duodenal Ulcer with Periduodenal Abscess	I-13-17	20	8	3	3	Golden, yellow, clear.	

TABLE IN CASES IN WHICH THE EXAMINATION OF THE DUODENAL CONTENTS WAS OF DIAGNOSTIC AID (May, 1916, March, 1918).—*Continued.*

Case.	Name.	Diagnosis.	Date.	Examination of Duodenal Contents.				Appearance of Duodenal Contents.	Remarks.
				Alkalinity.	Amylopsin. M. M.	Steapsin. M. M.	Trypsin M. M.		
23	Mr. J. K—	Hemolytic Jaundice and Cirrhosis of Liver	V-15-16	30	3	2	1	Greenish, yellow, turbid.	
24	Mr. A. S—	Hemolytic Jaundice and Cirrhosis of Liver	III-2-17	30	6	6	4	Yellow, brown, turbid.	

interest. In one the trypsin ferment was greatly diminished; in the second it was always entirely absent.

Case 21 is probably a milignant disease of the pancreas. In Case 22 the bile was clear and seemed to negative gallstone disease. For further particulars see the full case report (Case 5).

Another case of clear bile, not mentioned in the table, that came to operation is likewise of interest and helpful in excluding gall bladder disease. The patient, E. T., had three attacks of severe abdominal colic and gastric hemorrhages in the course of four years. During the last attack there was tenderness over the right abdominal side (gall bladder and appendicular regions). The thread showed no distinct blood stain, the bile was golden yellow and clear. The diagnosis of appendicitis was made. At the operation the stomach and gall bladder were thoroughly explored and found normal. The appendix was diseased and strictured. It was removed.

Cases 22 and 23 represent hemolytic jaundice; both were intensely icteric, but bile was constantly found in the duodenum, but was very turbid.

As seen from the table and the few cases described in full, the examination of the duodenal contents with regard to the appearance of the bile and the presence and quantity of the pancreatic ferments was often of importance and helpful in the making of diagnosis.

In a former paper I described a method of imitating the looks of the duodenal contents in such a way that an imitation sample can be kept in a record. Today I take pleasure in showing you a colored photograph of a number of samples of normal and abnormal duodenal contents (representing principally bile).

You can easily see the great varieties and deviations from the normal encountered in the duodenal contents in pathological conditions. It is principally the bile which produced these kaleidoscopic variations. Normally it is clear and golden yellow. In pathological states it is frequently turbid and greenish or dark brown.

The duodenal contents can be examined for a great many other items than those stated in the present table. Thus, the bacteriological and the microscopical examinations are of import. A great many other points, which I shall not broach here, will likewise have to be investigated. Even with the scant knowledge

we have at present at our command, the study of the duodenal contents (bile and pancreatic juice) is frequently of value in abdominal pathology. The direct examination of the duodenal contents deserves, therefore, to be more frequently employed in the field of internal medicine.

DISCUSSIONS.

Dr. Willy Meyer, New York City: Mr. President and Gentlemen: In the course of the last twenty-five years the laboratory has given us, in our attempts at refining the diagnosis of troubles on the border-line of medicine and surgery in the upper right abdominal quadrant, four useful methods: radiography, the Einhorn String Test, the cholesterol test, and the analysis of the duodenal contents.

Regarding the X-rays the majority will likely agree that the claim made by some of our radiologists that they are able to find positive results in gall stones in fifty per cent. of the cases, is rather too high. Fifteen (15) per cent. will, I think, come nearer to actual conditions. I am a firm believer in the value of the string test.

The cholesterol test, I think, had shown in about 70 or 80 per cent., a decided increase, if gall stones were found at the subsequent operation. Regarding the value of the examination of the duodenal contents I am sure that in this gathering it is not necessary to emphasize the great advance made, that we are able today to examine in the laboratory the secretions of liver and pancreas, as it is physiologically discharged into the duodenum. We can see color and turbidity of the bile, we are able to examine it bacteriologically. In our hospital, our serologist has made the diagnosis of typhoid carriers just from this one method. Dr. Einhorn has stated that in eight out of ten cases in which the bile was found to be turbid, gall stones were found at the operation. He also mentioned a point which we should not forget, that a stone may cause absolute occlusion of the cystic duct, and clear bile will then run from the liver direct into the duodenum. In making the more refined diagnosis in these cases, this examination of the duodenal contents has to be added in every case. We have made it a rule to do so. That it will show, incidentally, pancreatic disease, is evident.

I cannot go further into interesting details we have observed in our clinical experience. However, I would like to mention, in this connection, one class of cases, not pertaining to our present discussion, in the treatment of which the duodenal tube has been of great value, the so-called thromboangitis obliterans. I personally do not believe this disease to be one of the blood vessels, but of the blood itself. We have filled the system with nine to ten quarts of Ringer's solution every day, an amount, which no patient is able to swallow. Here the duodenal tube was of the greatest value. The patients read a book or the newspaper while the fluid enters by means of the rapid drop method, four times a day 2½ quarts. This, in many instances, proved to be of decided therapeutic value.

I would also mention another experience of great practical value made possible by the use of the duodenal tube. I have now under my care an obscure case of liver and gall bladder disease. I will not give you the details, but that patient, after excision of the gall-bladder, developed, at a secondary operation, a duodenal fistula. She was very low at that time. Every physician and surgeon knows that the formation of a duodenal fistula is a most serious complication, as the secretion will digest the wound. In this case the character of the wound and that of the skin were changed within twenty-four hours. Operative surgery would have been necessary to close up the fistula. But the patient would have died, if there had been surgical intervention. In this emergency we decided to introduce the duodenal tube and let its tip travel down as far as it would, following this up with duodenal feeding for several weeks. I am glad to report that this duodenal fistula has closed spontaneously, a fact, which I consider a decided progress in our therapeutic means.

DR. LICHTY: Dr. Einhorn's paper is open for discussion.

DR. THOMAS R. BROWN, Baltimore, Md.: I have been very much interested in duodenal secretions in pancreatic diseases, but I have approached the subject from the other point of view, and I have reported a series of such cases before this Association. I have made careful quantitative estimations of the trypsin and diastase in the stools, and can substantiate Dr. Einhorn's findings in cases of carcinoma and the trypsin diminution in the cases of pancreatitis. It was necessary first, to establish a normal. It gave us figures which were very definite. Our method gave us figures for these cases which we did not get in our normal cases.

After giving a definite amount of rest and a laxative the stools were collected, brought up to a definite amount with water and centrifuged. The trypsin and diastase were studied. Using twenty patients as normal, we found a definite low normal of six hundred units in the case of diastase. None of our normal patients fell below this. We had an opportunity of studying cases all verified by surgical operation. We had ten cases of pancreatic carcinoma operated on by Finney, and in these, expressed in terms of gram starch units, none showed more than twelve. In other words, the low limit of error. We have regarded this as of great value in diagnosing pancreatic lesions. There were only ten cases, but that is not a very small number, considering the rarity of the disease. There was no case in which diastase was present to any appreciable extent. In cases of pancreatitis, and here we are standing on debatable ground, we have seen a few cases in which we could not get away from the fact that there was a chronic pancreatitis. Dr. Finney was willing to commit himself as to this diagnosis. We did not have such low limits in these, that we had in the other cases. The quantitative estimation of these ferments in the stool is well justified, because if we have complete absence of pancreatic ferment below twelve units, or the low

limit of error, and if we can eliminate sprue and one or two other conditions, while we are not justified in diagnosing pancreatic carcinoma, we are at least justified in thinking of the probability of some distinct disturbance of the pancreas.

I have tried a few cases by Dr. Einhorn's method, but they have been too few to warrant conclusions.

Dr. John C. Hemmeter, Baltimore, Md.: The complicating factors of inflammations of the gall bladder, such as carcinoma and pancreatitis have been sufficiently dwelt on by Dr. Einhorn and Dr. Brown. I shall, therefore, confine myself to my experience in those duodenal chemic conditions in patients, which would be judged as gall stone cases strictly, without complication. The particular point I wish to emphasize in my cases is that I only took such cases as were found later, at operation, to be simply cholelithiasis, and studied them during a long clinical period. They were studied before and after operation, some of them for ten years. I have 24 such cases. Some I accompanied to Carlsbad and came back with them. In these patients in whom duodenal studies were made repeatedly, and bile obtained on numerous occasions, the duodenal contents being studied chemically and microscopically, I found this condition which Dr. Einhorn calls "*turbidity*," and which I prefer to call "*viscosity*." I prefer to use the viscosimeter in determining this quality. I found that the viscosity was increased in sixteen out of the twenty-four cases and in six further cases, and the bile was fairly clear, and the viscosity not above normal. In two, the duodenal contents varied. The contents were clear after four duodenal aspirations executed in eight days, and very viscous and opaque in three other aspirations on intervening days. As the viscosity could be completely removed by precipitation with acid and alcohol, I concluded that it was due to mucin. There were epithelial detritus from the duodenum and particles of gall-bladder mucosa and the chemical constituents of the bile. The chemical constituents of the bile are a more constant factor in duodenal secretions than the mere appearance of turbidity, and I wanted to find what this turbidity was due to. I think Dr. Einhorn's observations are valuable and should stimulate further study on this problem. In two-thirds of my cases, the contents were opaque. I found this twice in cases in which there were no gall stones found at operation, but a large duodenal ulcer with inflammation of the duodenum. Sometimes the gall bladder was found empty at operation but cholecystitis and cholangitis were evident. In these cases, the stones may have become dissolved, and their remnants have passed out through the common bile duct. The contents of the duodenum were studied by me with regard to the amount of mucin, the bacterial flora and the total solid residue, quantitative analyses made as to the composition of the stone, whether made cholesterin or bilirubin, or calcium bilirubin, etc., etc.

Dr. Max Einhorn, New York City, N. Y., closing: I have not much to add. I will only say, with regard to the examination of these

ferments, that I do not use Metz tubes. I use a method which resembles the Metz tube method. I have, I think, demonstrated it here to the Society. I have arranged for agar tubes. The agar serves to keep a solution, which we make up—say a starch solution and a hemoglobin solution, and we use a solution containing oil. We keep it in solid form at blood temperature. That is the idea, to have a column which is not fluid at body temperature. If you have that, and dip these tubes in the solution containing the pancreatic juice that you want to test, then the condition of these digestive processes, the strength of these ferments will be indicated by the amount of agar with the albumin, starch or olive oil changed. I have arranged for that. Then, if you apply this method all the time, it is an easy way of making a test. You have to use only a small amount of fluid, and simply put it over night in the incubator and look to see how much is changed, and keep track of it. It is an easy method to compare. If you make examinations in normal and in diseased conditions, you have a measure to go by. I spoke of the trypsin ferment in pancreatic and other conditions, and I think that we cannot say that because this ferment is absent, the others are absent. That is not necessary. The trypsin ferment of the pancreas may be present, and the other absent, and one may be present in a large and the other in a small degree. I said that trypsin was absent in pancreatitis but amylopsin was present. Dr. Brown tested the amount of starch for sugar. He found that particular ferment present in cancer of the pancreas. With regard to judging a disease of the pancreas by an absence of the trypsin ferment, it is understood that we will have conditions in which the pancreas is diseased, and still there may be an increase in the digestive power of the ferment, because there is at times hyperactivity present. It is just the same as in the stomach. We will have a stomach that gives normal secretion, and then have an ulcer in the stomach and find too much secretion. Why should this not occur in the pancreas? and it does. We have forms of diarrhea for instance, in which the pancreas is affected, and find a flow of pancreatic juice three or four times the normal, and also a juice that is twice as active as the normal. It is a condition of hyperactivity. It is not an atrophy of the pancreas, where all the things have disappeared already, but still the pancreas is diseased. So I only want to say that, for the present the tests which have been used abroad, and which have been applied to the case because the pancreatic juice could not be obtained easily, have been applied with a view to finding whether it is absent, but we have found too much activity in disease. If we study pancreatic conditions more closely and compare what we find with the actual symptoms we shall have a picture of disease after a while, but we cannot know by the first examinations things that we should—or, I mean that we cannot draw the conclusions which it will be possible to draw later on, after accumulated experience. We should gather material and compare conditions in life with the symptoms, and then we can say what is wrong.

THE MODERN TREATMENT OF GALL-STONE DISEASE AS AFFECTED AND CONTROLLED BY DUODENAL INTUBATION.

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History of the Clinical Recognition of Cholelithiasis.

(See J. C. Hemmeter in Sajous Analytic Cyclopedia of Practical Medicine, Seventh Edition, Vol. III, p. 275-276. Also Die Krankheiten der Leber, by Quincke and G. Hoppe-Seyler, in Nothnagel's Specielle Pathologie und Therapie, Band 18, p. 180-188.)

The Relative Frequency of the Formation of Gallstones in the Human Body.

There must be great variations in the relative frequency of the occurrence of gallstones, among different nations, and these variations depend upon the method used in ascertaining their existence, whether by simple clinical investigation, by operation or autopsy. One need only to look over the alphabetical index of the Journal of the American Medical Association to be astonished at the large number of contributions to this subject, and also at the varying figures given concerning the frequent occurrence of this disease. Barker, in his splendid new work on the Clinical Diagnosis of Internal Diseases, states that the per cent. of human beings found to have gallstones at autopsy is 5 to 10 per cent. This may serve as an American estimate. Scheel, in Ugerskrift for Laeger, November 30, 1911, gives 15 per cent., based on 2,753 autopsies. Pel, in his Krankheiten der Leber der Gallenwege, page 312, quotes Halk as finding gallstones in 29 per cent. of all autopsies, and he himself, in his observations on the autopsies on old women performed in Amsterdam, found 20 per cent. of cases of gallstones in cases which had given no symptoms of gallstones during lifetime. It should be added that Halk's material was composed of individuals over fifty years of age. In the article by Quincke and Hoppe-Seyler, already quoted, the

relative frequency of the finding of gallstones by twelve European pathologists varies from 2.4 per cent. to 29 per cent. The largest autopsy material is that of Poulsen in Copenhagen, who gives 91,722 sections with 347 findings of gallstones, making *3.7 per cent., but Poulsen states that only 9 per cent. of this material showed any symptoms during life.

Three things influence the figures obtained at autopsy. First, the punctiliousness and carefulness of the pathologist, and, secondly, the age of the patient, and, thirdly, the sex. Peters, at Kiel, found that in persons under thirty years of age the percentage of cases of gallstones was .62 per cent., between thirty and forty years 3.24 per cent., between forty and fifty years 4.44 per cent., between fifty and sixty years 6.98 per cent., between sixty and seventy years 9.53 per cent., between seventy and eighty years 13.02 per cent., and over eighty years 16.36 per cent. The figures given by Rother of Munich are: One to thirty years 3 per cent., thirty-one to sixty years 6.9 per cent., sixty-one and over 19.2 per cent. Schroder of Strassburg gives the following figures: Under twenty years of age 2.4 per cent., twenty-one to thirty years 3.2 per cent., thirty-one to forty years 11.5 per cent., forty-one to fifty years 11.1 per cent., fifty-one to sixty years 9.9 per cent., sixty and over 25.2 per cent.

Prevalence of Cholelithiasis in the Female Sex.

A perusal of the American publications cited in the Index Medicus and in the publications of the Journal of the American Medical Association evidences a unanimity of opinion that in the United States women are affected between three and four times as often as men, and this proportion between males and females appertains at all ages. The same is true of German statistics. Reinelt found in subjects between the ages of fifteen and thirty years gallstones in 1.3 per cent. of the men and 3.8 per cent. of the women. From thirty-one to sixty years the figures were 6.4 per cent. for men and 14 per cent. for women, while over sixty-one years the figures were 17.9 per cent. for men and 25.4 per cent. for women. For the years from 1901 to 1906, 386 operations were performed for gallstones at the Heidelberg clinic.

*(Foot Note. In the above statistics by Poulsen an arithmetical error must have sneaked in, for 347 does not constitute 3.7 per cent. of 91,722. I make out that to obtain this per cent. he must have had 3,393 cases of gall-stones at autopsy.)

Of these 46 were men and 340 were women; in other words, there were seven times more women than men. This difference is attributed to the sedentary habits of women, influence of tight lacing, repeated pregnancies and puerperal infection. These etiologic factors must have consideration in the treatment.

In speaking of the direct etiology we must consider everything which could produce stagnation of the bile-flow. Among these we must consider compressing clothing, insufficient bodily exercise, dislocation or compression of the bile-ducts by tumors, cicatrices. Among the causes which are little recognized I wish to call attention to one of which I have convinced myself repeatedly at autopsies, that is, enteroptoses, and gastroptosis especially. The displacement of the stomach may cause traction upon the hepatoduodenal ligament. This I have frequently seen at abdominal sections undertaken for gallstone. Another cause is dislocated or floating kidney. Then there seems to me to be a form of atony of the musculature of the gall bladder, which in some way is dependent upon the traction caused by dislocated abdominal viscera in enteroptoses. The tugging upon the splanchnic and abdominal branches of the vagus interferes with the reciprocal innervation that exists between the sphincter at the papilla of Vater and the musculature of the gall bladder. A close relationship seems also to exist between gallstone disease and pancreatitis.

As the successful treatment must be based on a knowledge of etiology, we must repeat the statement of Naunyn that two conditions are necessary for the formation of gallstones. *First,* stagnation of the bile-flow, and *secondly,* bacterial infection. Up to the present time this is still acknowledged to be an axiom, and was first pointed out by Naunyn in 1892, *Klinik der Cholelithiasis,* a brilliant classic on this subject. Throughout the many volumes of the *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie,* this eminent clinical philosopher has given us the benefit of his broad experience and conservative critical judgment. According to him, the modern era of cholelithiasis begins at 1892. The significant progress of surgical technique in this period is especially noticeable in the American literature on the subject, and this is so great and comes from so many able operators and surgical writers in the United States that I deem it inexpedient to cite their experiences in an article that is to be limited to the

purely medical treatment of this condition. But I cannot pass over stating one impression that I gain from American surgical literature, namely, that the so-called early operations have in general been given up, and that the special field for the surgeon is the chronically recurring cholelithiasis. Especial indications for operation are, *first*, the infectious cholocystitis, and *secondly*, chronic obstructions of the biliary ducts.

In my articles already quoted I have dwelt on the chemistry of cholelithiasis. The stones consist of cholesterin, calcium and pigment. The calcium occurs in the form of bilirubin-calcium, calcium carbonate and calcium phosphate. Bilirubin-calcium and the inorganic calcium salts are insoluble in the bile, but as normal bile never contains so much cholesterin that it could not dissolve still large amounts, it is probable that cholesterin stones can be dissolved to a considerable extent in human bile. Cholesterin is kept in solution by the bile salts and the precipitation of cholesterin from bile results from a withdrawal of these salts and by action of bacteria.

A remarkable difference of opinion exists between clinicians and physiologists concerning the derivation of cholesterin. Naunyn is of the opinion that the mucosa of the gall bladder furnishes the cholesterin, as well as the calcium, of the gallstones, and thereby furnishes an explanation of the local origin of the gallstones in the gall bladder. Physiologists, however, know that cholesterin is not formed by the gall bladder or the liver, but is very widely distributed throughout the body and that it is only eliminated by the liver-cells from the blood, which collects it from the various tissues of the body. Cholesterin is a constant constituent of the blood. That it is an excretion is illustrated by the fact that it is eliminated in the feces, but the contrary view has been suggested also, namely, that the cholesterin is in part re-absorbed and used again in the formation of new tissues. It is insoluble in water and dilute saline liquids. In the bile it is held in solution by salts of the bile acids. I wish to add in explanation of Naunyn's view that the cholesterin is formed by the mucosa of the gall bladder, that this has reference only to the inflamed gall bladder. It is, therefore, a pathologic production of cholesterin that he has reference to.

Numerous other American, as well as foreign authors, have investigated the production of gallstones by the intermediation of

bacteria. Most of them show conclusively that the presence of bacteria increases and accelerates the precipitation of cholesterin. Heyrovesky and Exner succeeded in producing a decomposition of the bile salts by the addition of typhoid (Eberth) bacillus and the colon bacillus. By this the cholesterin was also precipitated, because it is held in solution by the bile salts. Kramer succeeded in producing precipitation of cholesterin by inoculating animals with the typhoid and the colon bacillus, contained in tubes of bile bouillon cultures. Heyrovesky had arranged a scale of bacteria, graded according to the intensity and quickness of their effects. The organism which acts promptest and most intensely, according to this investigator, is the typhoid bacillus. The next in order is the colon bacillus, and the weakest in their effects are the pyogenic cocci, streptococci and staphylo cocci. His conclusion that the latter cocci could not be the primary and immediate infective agents in the formation of gallstones, but are by him supposed to be causative of the secondary or haematogenous infection of the gall bladder, is not confirmed by American investigations, particularly by those of Rosenow, published in the Journal of the American Medical Association, November 21, 1914, p. 1835, which we shall quote more fully in the following:

The Bacterial Flora of the Normal Intestine.

About one-fourth to one-third of the total dry mass of the feces consists of bacteria. That amounts to 4.5 to 5.3 grams in twenty-four hours. The character of food, though it may influence the variety of bacteria, has no influence on the quantity. According to Weinert, sour milk is capable of producing the amount of the bacteria to about one-half that above quoted.

Meconeum of newborn infants is sterile. After the first breast milk is swallowed there are bacillus Biffidus of Tissier—Bacillus Acidophilus. On cows' milk there are Bacillus Coli Communis and Bacillus Lacto-Aerogens (a few streptococcus), on meat there are Coli Gracilis, Bacillus Lacto Communis—specimen of yeast—Sarcinae and Bacillus Butyric Acidi-Bacillus Subtilis. According to Metschnikiff, the principal putrefactive bacteria are bacillus putrefactiens sporogenes, bacillus Welchii, Oppler Boas bacteria, bacillus of Hauser—Bacillus of Bienstock.

In considering the relative importance of the factors of stagna-

tion and bacterial infection in the pathogenesis of gallstones, two perspectives must be held in mind—*first,* the factor productive of the precipitation either of cholesterin or of bilirubin calcium; *secondly,* the particular species of microorganisms and its derivation. Among the normal bacterial inhabitants of the intestines above mentioned, only the streptococci, the bacillus coli and the bacillus Welchi come into consideration. Among the abnormal microbic invaders of the digestive canal we must consider the bacillus of enteric fever, the Eberth Bacillus, staphylococci, pneumococci and the tubercle bacillus. Mieczkowski found in twenty-three cases of cholelithiasis the bacteria coli eighteen times, either in pure culture or mixed with staphylo- and strepto-cocci. Chiari in twenty-two cases of typhoid fever found the typhoid bacillus in the gall bladder nineteen times. The injection of a culture of typhoid bacilli, without ligating the common gall duct, produced no infection. These experiments therefore demonstrate the necessary co-operation of the stagnation of the bile. In thirty-two cases of cholelithiasis, Létienne found the following bacterial infections: Bacillus Coli Com. eleven times. Staphylococci, seventeen times, Streptococcus twice, Pneumococcus once, Tubercle bacillus once.

That a progressive, infectious inflammation of the wall of the gall bladder and of the bile-ducts is necessary for the development of stones has been demonstrated by the experiments of Mignot (L'Origine Microbienne Des Calcules Biliare, Archives Generale de Medicin, Aout, 1898). The same experiments emphasize the factor of stagnation. Mignot filled the gall bladder of rabbits and guinea-pigs with sterilized cotton or gauze, into which he brought a drop of attenuated culture of a virulent colon bacillus, or staphylococcus. He then sewed the bladders shut with catgut. Three weeks later the bladders were again opened. They had now become thick walled and rigid. A thread 2 cc. long was passed through the wall of the largest end of the gall bladder, so that it remains freely suspended in the lumen. The wound was sewed up a second time. Six months later hard stratified stones consisting exclusively of cholesterin were found in more than one-third of the cases in the biliary passages of these animals.

If these special bacteria were introduced simply on silk threads or sand grains and thereby a more or less intense cholecystitis was created, a precipitation of the bile was produced, but the process did not lead to stone formation.

Next the bacterial infection, therefore, the most essential causative agent is a paresis of the musculature of the gall bladder and bile passages.

Derivation of the Chemical Constituents of Gallstones.

In the various surgical procedures that have been employed for the cure of this disease, the surgeons have had in view almost exclusively the question of infection and the bacterial causes. When a cholesystectomy is performed, this is the exclusive view that the operator has in mind, but another and equally important element demands consideration, if the views of Naunyn and Frerich's are correct. The former held that the cholesterin was derived from the epithelial cells of the gall bladder and Frerichs assumed that the calcium to which the bilirubin and the fatty acids are generally bound are not derived originally from the bile but are products of the mucosa of the bladder. If these statements were correct, the removal of the gall bladder would not only be urgently necessary for the purpose of removing the bacterial etiology and prevent the source of infection but at the same time to obviate the recurrence of deposition of calcium salts and cholesterin. Long drainage of the gall bladder may affect the same object.

The percentage contents of human bile in calcium phosphate is 1.7 per cent. (Jacobsen), and in fresh dog bile Hoppe found 0.04 per cent. of phosphate of calcium and 0.03 per cent. of carbonate of calcium. Therefore the percentage contents in calcium salts found in normal bile would be sufficient for the formation of stones without drawing in a hypothetical calcium and gallstone secretion by the gall bladder. Cholesterin and bilirubin calcium are both soluble in sodium glycocholate and also in alkaline liquids. Whenever the bile becomes acid in consequence of long stagnation, or abnormal secretion of gall bladder mucous, then the sodium glycocholate is split up into its constituents, namely, glycocol, cholalic acid, water and a sodium salt. The consequence is that bilirubn is precipitated as a calcium salt and then cholesterin, and eventually also sodium taurocholate precipitate. These processes can occur under the abnormal condition of stagnation.

A. Dochmann (Theorie der Gallenstein Bildung, 1889, Wratch No. 3, Abstracted from Maly, Jahrbericht, Band 20, p. 271) ana-

lyzed the liver bile and the gall bladder bile separately. The bile in the bladder was drawn after ligation of the cystic duct. In these separate analytic determinations he found considerable difference between the two samples. In the bladder bile the sodium was reduced and the potassium increased, as compared to the bile drawn from the hepatic bile duct. Now, the increased content of calcium reduces the solubility of the bilirubin and thereby leads to the precipitation of bilirubn calcium and of cholesterin.

In this controversy between those who hold that precipitation of bilirubin calcium and cholesterin from the bile as it comes from the hepatic duct is possible and those that hold that the epithelium of the gall bladder secretes these substances, a more recent pathologic and chemical study is of interest. I refer to the work of *Achoff* and *Bacmeister* (Die Cholelithiasis, Jena, 1909). These investigators believe that in most cases of inflammatory cholelithiasis there has been a non-inflammatory stage which preceded. They also set up the principle of different chemical origin of the different varieties of gallstones. They claim that *the radiated cholesterin stone* is formed *singly* and *exclusively as a consequence of bile stagnation and without the co-operation of bacteria,* but the cholesterin-pigment-calcium stone and the stratified cholesterin-calcium stone, as well as the pigment-calcium stone, are of inflammatory origin. These conclusions are based upon the following consideration:

Solitary Non-Infective Cholesterin Stone.

The structure of the radiated stone is purely crystalline. From a center of crystallization rods of unequal length radiate in all directions toward the periphery. These cause the uneven surface of the stone, which is very porous, contains an albuminous skeleton structure and very little calcium. This stone is found only in gall bladders that are not inflamed, simply in a state of stagnation. The morphology of this stone is indicative of *a very slow* process of deposition of its contents by crystallization from the bile. Its chemical composition corresponds to the composition of the normal bile, not of the bile changed by inflammatory processes. It is this type of gallstone that can be produced from the normal bile without infection by simple chemical decomposition. The radiated cholesterin stone occurs almost exclusively as a solitary stone.

Bacmeister experimentally proved that precipitation of crystalline cholesterin from stagnated bile could take place in the entire absence of bacteria or albumen. It is true this precipitation could be augmented by the addition of sterile epithelial cells. In these observations he found the proof that the cholesterin does precipitate from simply stagnated bile, not by infection but by sterile autochthonous decomposition of the bile itself, in which, of course, the protoplasmic elements participate.

The material for the formation of the solitary cholesterin stone crystallizes out of the sterile bile. The process is augmented by the scaling off of the epithelial cells of the gall bladder. By accurate investigations of gall bladders extirpated by operations or found at autopsy, they came to the same conclusion, namely, that when a single cholesterin stone was present every sign of inflammation of the gall bladder was missing and only the evidence of gall bladder stagnation was found. In order to arrive at this conclusion it was necessary to minutely study the anatomy and histology of the gall bladder, of which they give an admirable description. The distribution of the blood and lymph capillaries in the gall bladder and bile ducts is minutely described. They assign to the epithelium of the gall bladder a two-fold function: First, secretion of a pseudo-mucous substance (Nucleo-albumen) (?). The beaker cells secrete pure mucin. Secondly, the absorption of fat and pigment.

Naunyn and Fink had claimed that gallstones could be formed from Myelin, secreted by the epithelium of the gall bladder. This Achoff and Bacmeister deny.

In connection with the possibility of the recurrence of gallstones, after so-called cures, Achoff and Bacmeister call attention to the fact that the mucous glands, while they occur normally only in the neck of the gall bladder and in the cystitic duct, proliferate and extend throughout the entire gall bladder and into the walls of Luschka's ducts after inflammatory irritation. These ducts of Luschka extend into the musculature and fibrous tunic. The normal structure of the gall bladder undergoes certain changes in chronic cases of bile-stagnation. The normal folds are effaced. The muscularis is hypertrophied. A diffuse small-celled infiltration takes place, as a consequence of the increased resorptive processes. Especially the fat absorption is increased in a stagnated gall bladder. This leads to a dilation

of the sub-epithelial lymph capillaries. In consequence of this stagnation and the increased internal pressure the Luschka's ducts are dilated and often filled with a detritus of a bile-stained mass. On the base of this altered and stagnating gall bladder the solitary radiated cholesterin stone is formed.

The formation of inflammatory gallstones is entirely different from this.

Gall Stones of Inflammatory Origin.

The gall stones which are due to inflammatory conditions of the gall-bladder are the following: 1. Combination stones, showing interiorly the primary radiation of the cholesterin stone and exteriorly a stratified mantle rich in calcium. 2. The stratified cholesterin-calcium stones. 3. The cholesterin-pigment-calcium stones. 4. The larger oval barrel, or cylinder-shaped stones. 5. The common multiple faceted or mulberry-shaped stone. 6. The bilirubin-calcium stones.

Sometimes one can distinguish several cholelithic generations. It is sometimes also possible to trace different clinical pictures in the precedent history of gall-stone disease in connection with these different-shaped stones. The markedly crystalline and relatively calcium-poor stones grow slowly and occur as solitary stones. Those stones that are rich in calcium grow rapidly and are generally found in larger numbers. Achoff and Bacmeister assert that in the majority of all cases of cholelithiasis a non-inflammatory process precedes, and that definite relations exist between the different stone formations and the various diseased conditions of the gall-bladder.

As long ago as April, 1895, when I gave a demonstration of the first method for duodenal intubation practicable upon the human subject (see Hemmeter, Duodenal Intubation, Johns Hopkins Bulletin, April, 1895), I expressed the hope that the method might be available for the diagnosis of gall-stones from the chemical and physical conditions found in the duodenal contents. (See also Hemmeter, Diseases of the Intestines, Vol. 1, pp. 263-272. Also Hemmeter, *Versuche über Intubation des Duodenums, Archiv für Verdauungs-Krankheiten, Band* 2, *S.* 98, 1896. Also, *Archiv für Verdauungs-Krankheiten, Band* 17, *S.* 136, 1911.)

When one considers, however, the widely different chemical

composition of these various gall-stones and the different clinical history of each as above alluded to, one must be at once impressed with the difficulty of this kind of clinical research. If we are to determine from the bile aspirated from the duodenum not only whether there are gall-stones present, but their kind and the condition of the biliary apparatus, we should have reason to expect a different composition of the bile for each type of gall-stone. If in one case the stone is built up from the cholesterin of the bile, and in another case from the calcium, and in a third case from the bilirubin and calcium, it must be evident that we can expect no uniform and constant change in the bile that flows out into the duodenum under these conditions. This conclusion has been confirmed by my investigations, for all of my efforts to establish a constant chemical factor in the duodenal contents, and these efforts extend off and on throughout the last twenty years, have led to no definite chemical diagnostic factor discoverable in the bile as aspirated from the duodenum in cholelithiasis.

In an article entitled "Direct Examination of the Duodenal Contents (also Bile) as an Aid in the Diagnosis of Gall-Bladder and Pancreatic Affections" (*Amer. Jour. of Medical Science,* Vol. CXLVIII, pp. 490-495, 1914), Einhorn states that the microscopic appearance of the bile is of great diagnostic importance. If it is golden-yellow and clear, it usually indicates a normal gall-bladder. When it is greenish-yellow and turbid, it portends a diseased gall-bladder, which frequently contains gall-stones. He states that golden-yellow bile containing mucus is observed in catarrhal jaundice, but he admits that golden-yellow clear bile may occasionally exist, notwithstanding the presence of gall-stones, so his first conclusion is vitiated by the latter statement. But I would also add that sometimes greenish-yellow bile which is turbid can be drawn from the duodenum when the gall-bladder is not diseased, because the color may be due to a duodenitis and occurs also in duodenal ulcer. The remaining conclusions of this article refer to pancreatic disease and not to cholelithiasis. In only two instances do I notice a reference to the degree of alkalinity. In case No. 9, p. 492, the alkalinity is stated as equal to 20, and in case 16 as equal to 25. I presume this is expressed in terms of the titration method ascertained by 1/10 normal solution of NaOH. Now the chemical reaction of

the duodenal contents, when the hydrochloric acid of the stomach can be excluded, is due more to the alkalinity of the pancreatic juice than to that of the bile. I will later point out that this alkalinity of the duodenal contents is an important factor in the diagnosis, if it can be traced as due to the bile, which, of course, is exceedingly difficult. In the article from the *Archiv für Verdauungs-Krankheiten, Band* 17, P. 147, I described a case of varying gastric secretion to which I have given the term *"heterochylia."* This patient had periods during which no gastric juice was secreted, and other periods during which the gastric juice was either normal or excessively acid. When the total acidity of the gastric juice was normal, I found that it required 3.5 to 5 c.c. of $\frac{N}{10}$ H_2SO_4 to neutralize 10 c.c. of pancreatic juice. This patient had a small drainage tube inserted in a dilatation of the pancreatic duct after an operation for pancreatic cyst, performed by Dr. L. McLane Tiffany. The case is described fully by Dr. Harry Adler and myself in the *New York Medical Record,* for August 6, 1898, "A Chemical and Physiologic Study of Pancreatic Cyst Fluid." The case is cited here as a rare instance where the human pancreatic juice was studied during life and its alkalinity ascertained, but it was found that the alkalinity varied with the character of the diet. For complete date reference must be had to the original article.

So much must be evident: The alkalinity of the duodenal contents does not inform us concerning the alkalinity of the bile. If Einhorn finds an alkalinity of 25, this may be entirely due to the pancreatic juice. The bile itself, it is true, is alkaline, but only feebly so. Expressed by the above method, the bile that flows from the common bile duct during health has been found by me to be equal to 5, *i. e.,* 100 c.c. bile neutralized completely by 5 c.c. $\frac{N}{10}$ NaOH. Nevertheless, a marked diminution in the alkalinity of the duodenal contents is a significant sign of the presence of disease of the gall-bladder. Should the alkalinity fall below 5, we can assume that both the pancreatic juice and the bile are prevented from entering the duodenum. I have had two cases in which a persistent low alkalinity of this type was followed in from three to six weeks of jaundice.

In estimating the alkalinity of the bile the hydrochloric acid of

the gastric juice must as far as possible be excluded and the duodenal juice drawn at a time when the stomach is empty.

The most complete chemical study of the bile, from which most of my figures are obtained, is found in *Bottazzi's Chimica Fisiologica,* Vol. II, p. 401, *"Il Fegato e la bile."* The tables, Nos. 79 and 80, give the complete results of eight brilliant chemists on their analyses of the mineral contents and the organic contents of the bile.

Differences Between Gall-Bladder Bile and Liver Bile.

Liver-Bile is much less concentrated than gall-bladder bile. Determinations made on gall-bladder fistulas in man give a total solid residue of about 0.11, but this bile is not normal. They are due to the great loss of bile from the body, for normally bile makes an intermediary circulation, being reabsorbed from the intestine and excreted again from the liver. If it is lost through a gall-bladder fistula, this must lead to an impoverishment in solid substances. The liver-bile contains 3.21 to 4.66 per cent. of solid residue, according to Hammarsten, *"Ergebnisse der Physiologie,"* 4 Jahrg. "Chemie der Galle," p. 4.

The gall-bladder bile contains 15 to 17.03 per cent. of solid substances. There is a resorption of salts of the bile which takes place in the gall-bladder and bile-duct and simultaneous with this reabsorption of salts, organic bile constituents are secreted in the gall-bladder. The bile, if drawn at all from the duodenum, must be gall-bladder bile and even normally greatly different in its solid constituents and salts from the liver bile.

The gall-bladder also secretes mucous, which can be precipitated from human bile by alcohol. It seems to be a mixture of nucleo-albumin and mucin. The genuine mucin in human bile is derived from the bile passages and if there is a marked presence of mucous in the duodenal contents, it either speaks for duodenitis or for inflammation of the gall-bladder and bile duct. A marked diminution in the total solids of the bile, apart from the organic constituents, means that the calcium or the cholesterin or the bilirubin and pigments are being retained for the formation of gall-stones.

There is a stage of the cholelithogenic process where the stones, when completely formed, may undergo partial solution, provided the human subject still retains a fairly normal bile

secretion. In this stage the total solids of the duodenal contents may exceed the normal liquid from 3-15 per cent. It is known that gall-stones formed in man undergo complete dissolution when sewed into the gall-bladder of a dog.

There are, therefore, four diagnostic factors to be obtained from the chemical composition of the duodenal contents. *First,* diminution of the alkalinity. *Second,* increase of the mucin. *Third,* diminution of the total solid residue. *Fourth,* Therefore there may be a stage in the lithogenic process where the bile as it issues from the common gall duct (*i. e.,* in cases where the peri-cholangitis has not progressed far enough to prevent the issuance of the bile, partly or completely) contains more total solids than normal bile, the excess of solids being then mainly made up of Ca, Cholestrin, Bilirubin or a mixture of these according to the composition of the calculi. It is conceivable that there are cholelitholytic bacteria, *i. e.,* micro-organisms, that disintegrate already existing gall-stones.

It has been observed by Naunyn that gall-stones which were already partially disintegrated and dissolved when not expelled were reconstructed into new stones by the secretion of the inflamed gall-bladder mucosa, which is rich in Ca and bilirubin.

As regards the color, I should say that normal bile is always yellow, due to urobilin. A green bile is pathological.

Bacteriology of the Duodenal Contents.

If we have in view the factor of infection in a diagnostic study of cholelithiasis, the bacteriology of the contents of the duodenum can afford us very little aid, for even if the bile is excreted into the duodenum, the bacterial flora which we succeed in obtaining (if we obtain any) will be that of the contents of the gall-bladder and not of the gall-bladder tissues. E. C. Rosenow has perfected newer methods for the study of the bacteriology of various infections (Jour. A. M. A., Sept. 12, 1914, p. 903), and in the article, which I shall quote more fully, he pointed out that streptococci of a certain grade of virulence and from different sources are capable of producing cholecystitis and gall-stones after intravenous injection, and that large numbers of the cholecystitis constitute the nuclei of the stones.

Rosenow describes an interesting case in which cholecystitis developed in the sequence of an acute tonsilitis. The symptoms

began ten days after the tonsilitis and continued three weeks without jaundice. Then the pain shifted and jaundice began, which deepened for a week. Five weeks after the beginning of the attack Dr. A. B. Bevan performed an operation. There was found a healing area of necrosis at the fundus of the gall-bladder, which was moderately distended with bile containing mucous, and three mulberry cholesterin stones. Cultures made from the bile were sterile, but cultures made from the center of the stones developed streptococci, colon bacilli and the gas bacillus. An emulsion of the excised piece of tissue of the gall-bladder developed only streptococci. The culture and tinctorial properties of these special streptococci are given.

A dog was injected on January 22, 1914, with the growth of streptococcus from the wall of the gall-bladder, in 90 cc. of ascites-dextrose broth, suspended in 7 cc. of sodium chloride solution. On January 24th the dog was lame in the left hind leg, fluid from knee joint turbid. Cultures made. January 26th—cultures from knee joints showed four green-producing non-hemolyzing streptococci. January 30th—animal found dead. Acute cholecystitis, enteritis, pancreatitis, nephritis. The wall of the gall-bladder was edematous 3 to 6 mm. thick, cavity distended with brownish fluid. A plug of muco-pus stenosed the diverticulum of Vater. Pressure on the gall-bladder failed to discharge bile until this plug was removed by passing a probe and making firm pressure. A number of dark concretions of the consistency of putty were found in the muco-pus of the gall-bladder, and in the plug. The liver was normal. Kidney nephritis. The lower end of the small intestine was hyperemic large intestine, adrenals, heart and thyroid were normal. The bile, the plug, of mucous and the walls of the gall-bladder yielded large numbers of streptococci. The blood remained sterile. Sections of the wall of the gall-bladder showed marked thickening and degeneration.

This extremely thoroughly worked out case demonstrates, first, that a streptococcus tonsilitis may induce a cholecystitis and gall-stones in the same patient within three weeks; second, that a culture of streptococci gained from this patient and injected into a dog may produce acute cholecystitis, putty-like masses in the gall-bladder, a plug in the diverticulum of Vater causing complete obstruction, and death of the animal after eight days.

This contribution of Rosenow's is of such importance that I venture to abstract it in the following:

"The fluid contents of the gall-bladder, the center of stones, and particularly parts of the wall of the gall-bladder of twenty-nine cases of cholecystitis have now been studied according to Rosenow's new method, which was published under the title of "The Newer Bacteriology of Various Infections as Determined by Special Methods," in the Journal of the American Medical Association, September 12, 1914, p. 903.

"In five cases the cultures from the wall were negative and in these the microscopic evidence of any changes was slight. In the remaining twenty-four cases, in all of which increase in thickness and other changes were more marked, streptococci were isolated in all but three and in pure culture in ten. In sixteen cases streptococci were found in the wall when the contents were sterile or contained only the colon bacillus. The colon bacillus was found with the streptococcus in only ten cases, one in pure form, once in association with the bacillus Welchii, and once with staphylococcus. Bacillus mucosus was found in two cases of very acute cholecystitis. In two, diphtheroid bacilli were found and in one the fulsiform bacillus was found. The fluid contents, usually bile, were examined in twenty-six cases: In twelve it was sterile; streptococci were found six times, colon bacilli nine times; staphylococcus three times; the bacillus mucosus twice, and the fusiform bacillus once. The center of gall-stones have been examined in thirty cases. Only two proved sterile; from the rest, streptococci were isolated in all but three, fourteen times in pure form and five times in association with the colon bacillus; the center of the stone, in one case, showed the typhoid bacillus in pure form, while the center of two stones and the wall of the gall-bladder in a case with a clinical diagnosis of typhoid cholecystitis showed streptococcus in pure culture; in two cases the center of stones contained colon bacillus and the bacillus Welchii, and one of the latter organism only; in some instances streptococci were demonstrable in smear preparations from the center. Cultures from other portions of stones were usually sterile. The adjacent lymph-glands were examined in five cases. Streptococci were found in four, pure in three cases and in association with the bacillus Welchii in one case. In the cases in which a pure culture of the streptococcus was obtained

from the tissue of the gall-bladder there seemed to be a definite relation between the number of colonies which developed and the degree of change, especially if relatively recent inflammation was present.

"A comparison of the results obtained from the bile, the stones and the wall of the bladder, in the individual cases, shows that a bacteriologic examination of the fluid contents gives trustworthy results only in the acute stage of the disease; during convalescence and in chronic cholecystitis the results are of little value and may be misleading. In chronic cholecystitis the bacteriology of the center of the stones is similar to that of the wall of the bladder.

"The effect of the various organisms on intravenous injection has been tested in dogs and rabbits. All of the five strains of streptococci isolated from the wall of the bladder, one strain from an adjacent lymph-gland and two out of five strains from the center of stones showed a marked affinity for the gall-bladder soon after isolation, and frequently produced no lesion elsewhere. varying doses produced cholecystitis in nearly every animal injected. The severity of the lesions in the animals often corresponds to that found in the cases from which the strains are isolated. This affinity is soon lost, however, on cultivation as well as on animal passage. Five strains of colon bacilli, the one strain of typhoid bacillus, and one strain of the bacillus mucosus, in no instance showed any tendency to localize in the gall-bladder. It was not possible to produce cholecystitis with the streptococci by injecting them into the portal system, even with strains which produced cholecystitis practically every time when injected into the vein of the leg, and only localized cholecystitis developed at the point of puncture when the injection was made directly into the gall-bladder. In the animals which lived for a time there was not infrequently observed the beginning formation of gall-stones containing numerous streptococci similar to the conditions found in several of the patients.

"The strains of streptococci from the different cases show a striking similarity and resemble closely those from ulcers of the stomach. They produce either small, moist, grayish-brown or grayish-green, non-adherent, non-hemolyzing colonies on blood-agar; they ferment mannite, lactose and salicin; they produce short chains in liquid mediums with clumps of cocci somewhat

resembling staphylococci; they are of a rather low virulence, yet somewhat more virulent than strains from gastric ulcers, as manifested by their resistance to phagocytosis, by the smaller dose necessary to kill, and by the fact that, when cultivated for a time, they acquire affinity for the stomach and duodenum, while the strains from ulcers, when passed through one or two animals, acquire affinity for the gall-bladder at the same time as they lose affinity for the stomach.

"On animal passage, two of the strains produced both cholecystitis and pancreatitis, the lesions in the latter being most marked in the head of the pancreas.

"The lesions most commonly observed other than cholecystitis, when these strains are injected especially in rabbits, are: ulcer the stomach, hepatitis about the gall-bladder, myositis any myocarditis, arthritis, appendicitis and colitis.

"The common presence of streptococci in the wall of the infected gall-bladder and in the center of gall-stones, often in pure culture, while absent from the bile and their affinity for the gall-bladder in animals are strong evidence that streptococci are the cause of cholecystitis in man far more frequently than believed and serves to explain the good results reported by some as following cholecystectomy in cases of myocarditis, arthritis and other conditions."

As far as the diagnosis of the bacterial cause of cholecystitis from the contents of the duodenum is concerned, these studies of Rosenow are discouraging for the efficacy of duodenal intubation in this direction, inasmuch as the bacteria which have caused the cholecystitis are not present in the bile as issuing from the common gall-duct. They cannot even be detected in the blood, but were found only in the wall of the gall-bladder itself. The problem is more promising of solution when we are dealing with the Eberth bacillus of enteric fever. If this is the cause of the cholecystitis it is, as a rule, present in the bile coming from the common gall-duct, and it is this class of patient that constitute the so-called typhoid fever carriers.

The bacterium which is the cause of the gall-bladder infection cannot always be isolated from the liquid contents (the bile), although it may be from the wall of the bladder and the center of the stone.

It is not necessary to undertake puncture of the gall-bladder

through the intact abdominal wall, as Levy and Naunyn have done, in order to ascertain the specific micro-organism. This can be obtained by duodenal intubation, often gentle massage of the gall-bladder through the abdominal walls, by setting up of the bile evacuating mechanism by injecting HCl and albumoses into the duodenum.

In case there is an obstruction of the cystic or of the common gall-duct, this procedure cannot prove successful. It, is, therefore, necessary to first find out whether these ducts are permeable. The most practical method to ascertain this is the examination of the stools. If there is fecal Acholia, then duodenal intubation can bring no bile. I must add, however, that there have been two cases in my experience where I obtained bile in quantities of one-half to one and one-half cc., even when the chemic test and appearance of the stool gave no evidence of it. It is possible that the small amount of bile that reached the duodenum was reabsorbed before it reached the colon.

But if any bile reaches the duodenum at all it can be aspirated by the method of duodenal intubation, which was first practiced by me in 1897. Physiologically, the sphincter at the papilla of Vater opens only when the gastric chyme spurts into the duodenum, when the stomach is empty there is no evacuation of bile, but I will show later that this sphincter can be made to open by injecting a solution of hydrochloric acid and pepsin into the duodenum. It has been said that hydrochloric acid by itself will effect this, but it is more efficient if pepsin is added. *The most efficient substance to effect the relaxation of the sphincter* at the *common gall-duct is a filtrate of human gastric contents obtained from a normal individual.*

All of these substances have a certain degree of acidity which has to be ascertained beforehand to deduct the amount of their acidity in calculating the alkalinity of the duodenal contents after they are drawn. One cc. of normal gastric filtrate from a human individual will cause the evacuation of between 10 and 12 cc. of bile. A few drops of the HCl and pepsin solution suffice; these can be aspirated and the subsequent secretion used, which is, as a rule, free from the injected HCl.

The hydrochloric acid or the filtrate of human gactric contents thus injected causes the formation of the secretin from prosecretin, which in turn evokes the secretion of pancreatic juice, and

is supposed also to cause a secretion of bile, though not all investigators are agreed on this latter point. (See Falloise, quoted in Maly's "Jahresberichte de Thier-Chemie, 33, 611, 1904.")

The course to pursue in aiming at a treatment of cholelithiasis that is based upon the cause would be to first ascertain the specific bacterium which is causing the infection, and thereafter to obtain a serum by inoculating animals with this special strain of organisms. It has happened in one of my cases of chronic cholecystitis, with occasional attacks of high fever that followed three months after a severe streptococcic tonsilitis, that anti-streptococcic serum apparently cured the patient, for she has remained without symptoms for two years and two months.

The difficulty will be to secure the proper strain of bacterium which is doing the mischief, but I believe that with patient research by the method of duodenal intubation, and making use of the neuro-chemic mechanism which controls the sphincter of the common gall-duct, marked advances in the diagnosis and therapy of this condition will be made and the principal strain of the special pathogenic micro-organism be obtained.

The treatment of cholelithiasis has different aspects in view and varies according to the diagnosis of the condition present. It will also vary according to the causes of the conditions.

It is necessary to plan a special treatment for the following four conditions:

First. The gall-stone colic with the acute occlusion of the common gall-duct and the recurrent cholelithiasis.

Second. Inflammation of the biliary vessel and reservoir system (gall-bladder, cystic duct, the acute cholelithic cholecystitis) with its consequences; (*a*) Perforation peritonitis; (*b*) the diffuse cholangitis; (*c*) the chronic cholecystitis with empyema and dilatation of the gall-bladder.

Third. The invasion of the deeper bile passages by the stones —the chronic occlusion of the gall-duct. The differential diagnosis and management of the various types of icterus.

Fourth. The consequences and complications of cholelithiases —malignant neoplasm of the gall-bladder.

The principle of non-surgical treatment of cholelithiasis is to bring about a period of quiescent latency in the disease. Complicated infections and all factors that tend to stagnation of the

bile may have stirred up a dormant disease. Of course, this can be treated by operative removal of the gall-stones and draining the gall-bladder. From what we have seen in the preceding, however, only 5 per cent. of all gall-stone carriers ever have symptoms. This makes it clear that there must be a great majority of cholelithiasis that harbor their stones throughout life, with a comparative degree of comfort, or are not aware that they have gall-stones.

I am not all opposed to the operative treatment of gall-stones. On the contrary, I favor it. (See article on Cholelithiasis, Analytical Cyclopedia of Practical Medicine, Volume 3, Page 295.) I also there call attention to the technique and value of duodenal lavage, in the treatment of cholelithiasis. L. C., page 201. But there are plenty of patients who refuse to be operated, or who never have a second attack, or who have been operated already and in whom the cholelithiasis returned, such cases, in short, that demand non-operative treatment.

For the present I shall pass over one of the most effective therapeutic methods of the internists, namely, the treatment by hot mineral waters and diet.

I wish to emphasize what I have repeatedly condemned, namely, the employment of so-called cholagogues, especially a number that appear to be proprietary articles. These are Eunatrol, which is acid-sodium-oleate; Cholelysin, which is also sodium-oleate; Gallisol (composed of sublimated sulphur, castor oil and tar); Cholagen, which is a combination of mercury, podophylin and ethereal oils.

Any agent that causes an hemolysis of R. B. C. increases the flow of bile, and the same effect is produced if a solution of hemoglobin is injected directly into the blood. The bile pigments are excretory products of hemoglobin. Most all so-called cholagogues are hemolytic and also protoplasmic poisons to the hepatic cells.

The use of olive oil, either by mouth or rectum, in large doses has, in my experience, not been followed by gratifying results. It has been claimed that concretions can be found in the stools after the oil treatment, and that they are the result of broken-down gall-stones. I have convinced myself that these concretions are nothing but fat conglomerations and that the large doses of olive oil, as given by Stewart and Mays, derange the digestion.

It would be pardonable if a slight improvement followed the treatment with the substances which I have just mentioned if we were sure that they did not do harm. Cholelithiasis is such a complicated and variable disease that improvement frequently follows by rest in bed, hot Carlsbad or Bedford magnesia water, and hot applications over the liver.

It is entirely irrational to speak of a solution of gall-stones by medical means. What the cholagogues are supposed to do is an increase in the flow of bile, in order to wash out the biliary passages. If it were really possible to increase the *secretion* of bile, it is not at all proven that an increase *flow* of bile through the gall-bladder, common gall-duct, and into the duodenum would follow. It is not sufficient to increase the amount of bile secreted. What is needed is an increased flow of bile through the biliary vessels. This is in the normal individual prevented by the sphincter of the common gall-duct. In 1887 Oddi showed this sphincter anatomically, and he also demonstrated that it is controlled by a group of ganglion cells which regulate the constriction and relaxation of the sphincter. (See illustration in Luciani's Physiologia del Uomo, Vol. 2, pages 187 and 188.) The same sphincter was studied by Hendrickson, Johns Hopkins Hospital Bulletin, September, 1898. Oddi found that the force with which the sphincter closes can only be overcome with a column of water of 700 mm.

Freese (Johns Hopkins Hospital Bulletin, June, 1905) found the force of the maximal contraction of the muscle of the gall-bladder to be 220 mm. of water; almost the same pressure was found by Haidenhain. This pressure varies according to the animal experimented upon, and Naunyn assumes that the force with which the sphincter of the common gall-duct is kept closed is equal to a pressure of 700 mm. of water. This is Oddi's estimation. Such a pressure is and beyond greater than could be overcome by an augmentation of bile secretion, for the secretory pressure of the human bile apparatus do not go beyond 250-300 mm. of water. Whenever the pressure in the bile ducts exceeds this the hepatic cells no longer secrete into the gall-ducts, but any bile that is formed is received into the lymph vessels which surround the hepatic cells, and eventually reaches the thoracic duct.

The reciprocal neuro-muscular control between the sphincter

of the papilla of Vater and the muscle of the gall-bladder can only be set up normally by the products of gastric digestion and in such a manner that the sphincter at the orifice of the common gall-duct is inhibited when the gall-bladder contracts and *vice versa.* To produce an increased flushing of the gall-ducts and gall-bladder with bile the sphincter of the common gall-duct must be opened. Physiologically this occurs during gastric digestion and evacuation through the pylorus. Assuming that cholagogues could augment the formation of bile, as yet there is no evidence that they can open the sphincter of the common gall-duct, the tonus of which will remain 400 mm. of water pressure higher than the pressure of bile secretion.

Gall-Stone Disease—Diagnosis.—When a cholelithiasis is already established diagnostically, on what ground can a chronic obstruction of the common gall-duct be assumed to exist?

In deciding this point the PATHOGENESIS OF ICTERUS calls for consideration.

It is an old error that the icterus of cholelithiasis must be an OBSTRUCTION ICTERUS. This jaundice is most often due to an inflammatory state of the biliary vessels; it is an INFECTIOUS CHOLEANGITIS, which can exist without inflammation of the larger bile ducts. Chronic icterus may occur in CHOLELITHIASIS where no stones have left the gall-bladder —without stones in the larger ducts. And, *vice versa,* icterus may be ABSENT, although operation or autopsy demonstrates advanced obstruction of the ductus communis choledochus.

It is also possible in cholelithiasis to have icterus without acholia of the feces.

Feverless jaundice, with sudden exacerbations accompanied by high fever without severe pains, is a syndrome that is indicative of obstruction of the ductus communis choledochus with stones (Ehret). Both the increase of icterus, as well as of the fever, are due to a flaring up of a pre-existing choleangitis. A stone in the common gall-duct favors the invasion of bacteria at the duodenal end of the duct—the passage for the bile is usually not completely blocked. A stone in the diverticulum of Vater may still let out a little bile and may also let in many bacteria, hence the sudden "FLARE-UPS" of the infectious choleangitis.

Diagnosis of Cholelithiasis by Radiography and Radioscopy.—Cholesterin stones and the commoner stones contain, as a rule,

less than 0.5 per cent. calcium and cannot possibly give a shadow by the X-ray method. But there are stones that contain 20 to 21 per cent. calcium and these may give such a strong shadow as to be seen through the most concentrated bile. Bile itself gives a shadow.

A stone containing 11.56 per cent. calcium gave no shadow in the gall-bladder of the patient, but after cholecystectomy and removal this stone on being held on the same patient's abdominal skin gave a distinct shadow. In the gall-bladder it gave no shadow because the shadow of the bile itself screened it, the bile being a denser obstruction to the passage of the rays than the stone.

DR. MAX EINHORN, New York City: I was very much interested in Dr. Hemmeter's paper.

I only suggested inspection of the fresh bile as the easiest way to ascertain some points. But I have myself examined microscopically almost every case, and I have in that table a great many of them. We do find some minute particles of concretions. We find a great deal of bacteria. Years ago, when I started these examinations, I had systematically undertaken to have every duodenal contents examined by Dr. Garbat (?). At that time typhoid bacilli were found in one of my patients, and I myself cannot do that kind of examination. It is always advisable. There is no doubt that there are a great many things which are of importance, and which will have to be studied and an analysis made of them, and so on, and they are not so easy. But I took first the easiest which struck me as of importance, and if you find the bile turbid, it is of significance. We do find also something that is quite natural, a changed bile, an abnormal bile, in diseases of the liver. That certainly comes first. I remember a case of echinococcus cyst of the liver that we had in the hospital some years ago. In that case the bile was very turbid and green. There was no disease of the gall bladder, but the liver had a beginning cyst. I think Dr. Meyer operated on that case. He will remember that it was mentioned in one of my earlier papers. We must first know that there is no bad disease of the liver which does that, and then we can come to our conclusions regarding the other things. We have always to feel our way. If the duodenal alone is diseased, we, again, will find something wrong with the duodenal contents.

Another thing is that if we find a disease of the liver that should bring about a change in the bile, we shall always be able to predict the condition of the bile. If we have to deal with gall bladder disease, we may, at times, get bile that is good, because sometimes it comes directly to the duodenum, without going through the gall bladder. But all these things are of importance, and I am thankful to Dr.

Hemmeter and Dr. Meyer for mentioning other things, and to the other gentlemen for discussing these things.

Dr. John A. Lichty, Pittsburgh, Pa.: Does anyone else wish to discuss this paper? If not, I should like to have the privilege of discussing it myself for a few moments. The matter of focal infection in relation to disease, we have not heretofore recognized or fully appreciated. The idea is so attractive that we are likely to be carried away with it, and I have had in the last few months a practical experience that is confirmatory.

Two patients with definite gall-bladder symptoms had very bad infections of the mouth. They had tenderness over the gall-bladder with other definite symptoms. The dental surgeon corrected the condition in the mouth in both cases, and within a few days they were relieved of their symptoms. They were intelligent patients and knew about the relation of diseased teeth to infections elsewhere. You could asily say that you had demonstrated through these two patients that the gall-bladder disease was due to the condition in the mouth and yet we need a great deal more evidence before we come to so rapid and sweeping conclusions.

The question of the use of X-ray in the diagnosis of gall-stones is very interesting. In a symposium which we had in this Association three or four years ago the most conservative opinion was that of Dr. Baetjer, who found that in 16 or 17 per cent. of cases he could make the diagnosis of gall stones. I find, in conference with roentgenologists, that they are inclined to form their judgment on three points. One, of course, is the gall-stone shadow. Another is the presence of adhesions as shown by pulling the stomach over to the right or by producing a peculiar deformity of the duodenum. The third is the visualising of a dim shadow of a distended gall-bladder. I have followed these points at operation and have not found them reliable. What appears to be a gall stone is sometimes an artefact, and the position of the stomach may change very easily when no adhesions are present. And the "visualised gall-bladder" is frequently an airy nothing, evidencing only a keen enthusiasm. One point on which I have relied in X-ray in gall-stone work in the process of exclusion. If there are definite abdominal symptoms and you have excluded, by X-ray, almost every other possible condition, then probably there is gall-bladder disease. I have had a very definite jolt in this idea during the past month, however. Our roentgenologists in Pittsburgh have utilized the well-known action of belladonna on the nonstriated muscle of the stomach in their X-ray work. Where they find a "filling defect" they are not willing to make a diagnosis until they have the patient thoroughly under the influence of belladonna, to see whether they cannot smooth or "iron out" the defect wherever it may be. I had two cases that pointed to gall-bladder trouble and found the filling defect in both and ironed them out. One of them afterwards, while at work, had a very definite hemorrhage of the stomach, and I feel sure that that patient has a peptic ulcer.

So we ironed out something in this case that probably should not have been ironed out. The second case was a very definite one in which there had been gall-bladder symptoms eight years before, and during the last three years there had been hunger pains and symptoms that pointed strongly to peptic ulcer. We found the filling defect and ironed it out. I went to this patient and said, with a great deal of assurance, "Your trouble is gall-bladder trouble, and with your history I think it best to open the abdomen and correct what we find." The surgeon agreed to this. We opened the abdomen, and found a definite chronic ulcer in the pylorus, and the gall-bladder normal. Se we again ironed out something that should not have been ironed out. So I again come back to Baetjer's opinion that probably in 16 or 17 per cent. X-ray work is to be relied upon. In the others X-ray does not give any definite information, so far as gall stones are concerned. However, Dr. Hemmeter has given us points this morning which we must take home and digest, and apply in our work in the coming year.

Dr. Martin E. Rehfuss, Philadelphia, Pa.: When I was at Paris, I was much impressed with the work of Chauffard, whom I had the pleasure of knowing. I saw his wonderful work on the etiology of gall stones, and I consider it to be one of the most instructive works on the subject, the one he published. At that time his conception, which was not new, was that there was a distinct alteration of the cholesterol metabolism of the body. We have one chemist at Jefferson who devoted nearly all his time to the investigation of cholesterol. He uses the method of Autenreith and Funk in which 2 c.c. of blood can be examined for its cholesterol content.

I have been teaching that the stone is due to three factors: (1) a stasis of bile, probably best explained by method elucidated by Dr. Meltzer and mentioned by Dr. Hemmeter, stasis through the mechanism of Odi's (?) sphinctre and the smooth muscle of the gall bladder. Meltzer pointed out that if we miss a meal in the middle of the day, there will be undue stasis of bile, and that the best cholagogue was peptone. While I am going over old ground, I think that it is worth while to mention some of the things that Chauffard pointed out. One is the average cholesterol in an individual rises in certain forms of gall stone disease. We have been investigating many individuals, and have found that in operatively demonstrated stone, there is an increase of cholesterol in almost 80 per cent. of the cases. In our first series, we got a higher percentage. I attended operations, and found a low cholesterol with many stones present in six or seven cases of this kind. There were some with many stones that were without an increase of cholesterol. Probably during the formation of stone, there had been an increase of cholesterol, but the active formation of stone had passed.

Regarding this cholesterol mechanism, Chauffard pointed out that there was a positive increase after certain diseases. The formation of stones in typhoid fever, for instance, he thought was not due to

the fact that we have a residual typhoid carrier, but to cholesterol rise, and following the active stage of typhoid fever, we have an increase of cholesterol. Towards the latter part of pregnancy, also, there is an increase of cholesterol, which is followed, on the second day after delivery, by a drop, to be subsequently followed by a rise. Chauffard contended that gall stones owed their primary mechanism, not to gall-bladder disease, but to disturbance in the liver cell, which was responsible for making bile, and was deficient in substances incapable of holding cholesterol in solution.

As to the origin of cholesterol, it is claimed that cholesterol comes into the body by the food, exogenously and endogenously by body metabolism. We analyzed the food in high cholesterol cases. We could reduce the cholesterol by a low cholesterol diet. Then there is an endogenous formation of cholesterol through so-called cholesterogenic organs, such as the suprarenal capsule and the corpora lutea. There is then the question of infection. We have attempted to culture bile for the last two years. We do it almost every day. We use agar, serum and bouillon. I realize that the mechanism seems defective. We wash them out with simple water, using the syphon method. I realize that the results obtained by this defective method are not reliable, yet in almost every instance, we get a culture and the colon bacillus is very frequently found. Adami (1) claimed that the colon bacillus was normally passed through the bile, and in many cases I have seen it in the cultures obtained from the bile. We have had a number of cases of mixed infections with bacillus pyocyaneus and streptococci, and have found the colon bacillus very rarely. (?) In spite of Rosenau's studies, we have been unable to isolate it, except in one or two instances. We have 130 or 150 cases that we have cultured. These cases show the connection of infection and the alteration of bile, as shown in changes in the cholesterol content.

DR. LICHTY: Dr. Hemmeter's paper is now open for discussion.

DISCUSSION ON DR. HEMMETER'S PAPER.

DR. JACOB KAUFMANN, New York City: In the most interesting paper which Dr. Hemmeter has presented to us, the point which interested me particularly was the remark that the acidity of the gastric juice controlled the opening of the sphincter at the outlet of the common duct. Perhaps Dr. Hemmeter remembers that as long as 15 years ago I read before this Association a paper on gastric hyperacidity and gall stone disease. At that time the general conception was that gall stone disease reflexly produces increased gastric secretion. I think I was the first to point out that under certain conditions disturbances of gastric secretion may bring on gall stone attacks through the irritation of the duodenum by the acid gastric contents which may upset the mechanism of opening and closing of the sphincter, in the same manner as increased gastric secretion through the irritation of the duodenum interferes with the proper opening and closing of

the pylorus. The observation of Dr. Hemmeter corroborates this view. Further observations have shown that when gall stone disease has lasted a certain length of time, it is the rule that we find a much decreased, and often a complete absence of gastric secretion.

Dr. Hemmeter spoke about cholagogues, and said that this instillation of gastric juice into the duodenum acts as a cholagogue. This corroborates a statement made by Naunym, who examined every remedy and every method that was said to act as a cholagogue, and came finally to the conclusion that none of these acts as a true cholagogue. He found that there is only one thing that acts as a cholagogue, and that is a full meal. This would corroborate the idea of introducing gastric secretion into the duodenum.

As to the different constituents of gall stones, this is a most interesting topic, but I should like to ask Dr. Hemmeter how he would account for the findings of those men who have really examined the formation of gall stones, such as Naunym and Aschhoff. Aschhoff differs from Naunym and has a peculiar conception of the primary formation of stones, claiming that in each case the primary stone is formed by a sudden deposit of cholesterin. He says that even aside from the solitary cholesterin stone, in all cases there is a primary cholesterin stone, located at the neck of the bladder, no matter how many other stones of different composition fill the gall-bladder. He claims that this primary cholersterin stone is formed when there is a great increase of cholesterin in the blood, as f. i., in pregnancies, and that the other stones are formed afterwards, as Naunym claims for all stones, as the result of bacterial infection and catarrhal conditions. The question is, how would you be able, when this first chemical disturbance that caused the formation of stones has taken place twenty or twenty-five years before you see the patient, to distinguish by examination between the different constituents of stones in a given case? That is not quite clear. As I understood Dr. Hemmeter, he looks at it in this way: that the formation is a progressive affection which perhaps occurs periodically. I must say that I was much influenced by the teaching of Naunym, in whose laboratory I worked, sitting next to him when he was engaged in examining the formation of gall stones. He always pointed out that even if you get five or six hundred stones in a gall bladder, that they are all of the same age. Their faceting shows that. The mass has grown out of the fluid at a certain time, and the stones have pressed against each other, their faceting being brought about in this way. If that is true,—that the stones are formed at a certain period, and that whatever else follows afterwards, is, as Naunym claims, brought on by reinfection of the gall bladder, either by ascending processes from the duodenum or by secondary infection from the blood,—then I do not quite see how Dr. Hemmeter will be able to distinguish between the different types of stones.

Dr. C. R. Jones, Pittsburgh, Pa.: As to Dr. Hemmeter's observations with reference to the stones being formed without a bacterial focus, I should like to call attention to a number of cases in which

stones have been removed, and yet stones continue to be discharged through the ducts. I have seen one liver at post mortem in which a cross section showed every duct of the liver to be packed full of small stones. I have seen but one such case. That was in 1900. It has always come to my mind when thinking of gall stone conditions. We, of course, rightly refer to the stone as forming in the gall bladder, but here was a case in which the liver was completely packed full of these small, sharp-edged stones. They would really give you the idea of being stellate, with their sharp edges.

A question that I should like to ask Dr. Hemmeter is whether or not the administration of human gastric juice might be avoided by producing in the patient's stomach some psychic juice by the putting of food before him, or by some other method, so that he can furnish his own gastric juice for the opening of the gall bladder.

Dr. John C. Hemmeter, Baltimore, Md., closing: In the first place, I wish to thank the various members of the society for their very stimulating discussion, which has been most instructive to me. I knew Dr. Kaufmann had been a pupil of Naunym. For a good many questions, I have to refer you to the original article, because, in the time allotted to me, I cannot explain all the questions asked. The cholesterin question is extremely important, and I will try to answer some of the more important questions.

The question of Dr. Kaufmann, whether the distinction between the different kinds of stones was possible where there was a wide variation in their chemical condition, is one of these. He mentioned Aschoff and Backmeister (?) studies showing that there was a non-infective stone which might be ————. They are convinced that this is not inflammatory. It is indeed very difficult to arrive at any conclusion regarding the chemic composition of the stone, from the chemical analysis of the duodenal contents. But within wide limits of analytical results we can arrive at approximate conclusions. For example it is possible if we get enough duodenal contents to determine the amount of calcium or the amount of cholesterin and any excess above the average amount is indicative of gall stone.

Dr. Jones brought up a very interesting case, which he had seen. The liver and gall passages at a demonstration by Virchow. This case is interesting in connection with one that Hans Kehr (?) reported. In Kehr's case, for six months after operation stones drained out through the open fistula. The same preparation was demonstrated to me personally at the Pathol Institute in Berlin.

In my opinion this permits of the deduction of a descending or metabolic cholelithiasis. I believe that the process does not start in the gall bladder in these cases, but in the liver, and the stones come to the gall bladder already formed. The surgeon should join hands with the internist in these cases because after he has taken the stones away, the liver metabolism must be regulated back into normal condition and this requires an internist's experience.

Dr. White inquired whether the total residue calculations were not vitiated by there being so many other factors. That is one of the

difficulties. You have to contend with pancreatic juice and mucus, and as the pancreatic juice is alkaline, and as the alkali in the ash leaves residue, it is hard to get at exact deductions. I was anxious not to give all analytic tables that I had completed (?) in our clinic, but just enough to start a discussion. Finally—after a year of this chemic analyses I found that it is, instead of going into complex case analyses, to determine mainly the total solid residue. Any excess or marked diminution of solid residue of duodenal contents is indicative of gall stone disease, either in the formative (diminutive) or disintegrative (excess of residue) stage.

Dr. Einhorn correctly said that he did not draw conclusions alone from turbidity. I prefer to call that viscosity, because that is a conception of the physical chemistry, as viscosity can be determined by an instrument, the viscosometer.

Dr. Rehfuss, quoting the work of Chauffard, made me recall an exceedingly brilliant investigation on liver work made by Arnold and Glénard. It is a classic.

With regard to the cholesterol question, brought up in connection with that of Dr. Rehfuss's determinations by Andrews' and French's method, (?) I could remark that cholesterol is a normal constituent of the blood, and we must find out if increased at what point it should be considered abnormal. The gall stones occurring in pregnant women have received a new interpretation as regards their pathogenesis. In numerous pregnant women excessive cholesteremia has been formed. This altered blood metabolism is supposed to produce cholelithiasis of the cholesteral stone type.

As to the radiographic diagnosis, I would say that I read a paper before the society several years ago, in which I said that I had placed seven gall stones, one behind another, and photographed their combined thickness, and yet had got no shadow. Any stone, in order to give a shadow, must have calcium in it. It is the calcium that gives the shadow.

Captain Bryant asked whether the cholelitholytic bacteria could be used therapeutically. This is a problem for future experimental study. There is a medical treatment for cholelithiasis. I asked some students what the medical treatment of it was, and they said that there was none, and that the only treatment for it was operation. The surgeons had taught them to believe that. The bile can be got sterile by means of hexamethylenamin, tetramine, atropin (?). Salol will also get the bile fairly sterile. There is another prospective treatment, and that is, in these cases in which the cholelithogenic process is the result of infection of known origin (for instance, tonsilitis), the giving of an autogenous serum. These cases that have been operated on should be treated subsequently with a serum derived from the micro-organism found in the stone or in the wall of the gall bladder. The Carlsbad treatment aims at a solution of the stone by the hot Carlsbad water treatment which acts on the metabolism of the liver. In metabolic cholelithiasis it is most effective and has in my experience given three years' relief in 12 of my patients who had recurrent gall stone attacks after having been operated.

PRIMARY CARCINOMA OF THE GALL-BLADDER.

An Analysis of Twenty-three Proved Instances of the Disease.

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CHICAGO.

In the series of 1,000 operatively and pathologically demonstrated instances of gall-bladder disease, which I reviewed a year since, there occurred 31 cases of malignancy (3.1 per cent.). Of these gall-bladders the neoplasm was primary in 23. In the remaining eight cases the gall-bladder was secondarily invaded by extension of malignancy from adjacent viscera. There occurred no instance of primary neoplasm of the bile ducts. It is thus evident that of a large series including gall-bladder affections of nearly every type primary malignancy arose in 2.3 per cent. The practical value of this rate of the incidence of gall-bladder neoplasms is indicated by the observation that it is more than four times the frequency of primary malignancy of the appendix and that of neoplasms involving the organs concerned with digestion the gall-bladder is involved fifth in frequency (1, stomach; 2, colon and secum; 3, rectum; 4, oesophagus; 5, gall-bladder; 6, liver; 7, appendix).

It is frequently stated that the diagnosis of primary malignant disease of the gall-bladder is not difficult. This statement holds true for instances where there is extensive involvement, where pronounced general constitutional upset has occurred and where the prognosis is evident to even a layman. That there are actual difficulties concerned with the accurate diagnosis of primary neoplasm of the gall-bladder is proven by the fact that of the 23 cases in my series in but seven instances (30.4 per cent.) was the unqualified pre-laparotomy diagnosis correctly made and recorded on the histories and operation cards. In no case where early, well-localized gall-bladder malignancy existed was there a correct pre-operative diagnosis. It would seem, consequently, that the clinical diagnosis of curable neoplasm of the gall-bladder

occupies a status relatively similar to that of the clinical diagnosis of early, curable primary gastric malignancy.

On account of the foregoing observations it is considered that a clinical analysis of the 23 instances of primary gall-bladder malignancy included in my series of established gall-bladder disease will not be altogether valueless.

Sex.—It is commonly recorded that females are affected approximately three times as frequently with malignant disease of the gall-bladder as are males. (Musser, Zenker, Siegert, Mayo, Moynihan, *et al.*) From this observation it is usually deduced that because the incidence of gall-stones in females is about three times that in the male, gall-stones must of necessity be the cause of gall-bladder neoplasms. In spite of many successful experiments in the production of gall-stones, there is no instance on record where the deliberate experimental production of the calculi nor the accidental arising of such a consequence of foreign body (ligatures, drains, etc.) resulted in malignant disease—and this in spite of the fact that the so-called "irritant" has lain even for years in a previously healthy or diseased gall-bladder—(Homans, Jacques, Meyer, Mignot).

In our series of primary malignancy of the gall-bladder there were 16 males and 7 females.

Age.—The average for my series was for both sexes 59 years. The minimum age in males was 44 years, the maximum 76 years (average, 57.9 years). In females the minimum age was 56 years and the maximum 72 years (average 62.2 years). It would seem that in spite of the greater prevalence of gall-stones in the female, the average age at which malignant disease of the gall-bladder occurs is more than five years later than in the male.

Heredity.—There was only one patient of the series in whom a definite blood-relationship of malignancy could be elicited. In another patient the husband had died about a year previously from cancer of the stomach.

Duration of Symptoms.—In the 100 cases of cancer of the gall-bladder which Musser collected from various non-related sources and from the literature in 1889 the average duration of the ailment is stated as 6 2/3 months, with a minimum duration of seven weeks and a maximum of four years. It is quite evident when one analyzes cases that in numerous instances the patient has been affected with a gall-bladder dyspepsia of two distinctly

definite types, *viz.*—(*a*) a clinical form, not that commonly considered malignant, and (*b*) a terminal complaint frequently evidencing such serious local and constitutional disturbance as to render a suspicion of some malignant process being highly probable. There were in my series 16 cases (69 per cent.) where a previously harmless type of gall-bladder dyspepsia had been followed by an alarming complaint. In the early period the ailment was commonly intermittently manifested and extended in the average over 9.6 years (minimum 3 years, maximum 36 years). The terminal phase of the disease was one of continuous malfunction (often, clinically, on the part of the gall-bladder) and in duration averaged 10.3 months (minimum 5 weeks, maximum 3 years).

Of the 7 cases where from its inception the affection had been of an obstinate and progressive type the duration averaged 3.4 months (minimum 6 weeks, maximum 6 months).

It would seem that consideration of these two types of dyspepsia, ultimately proven to be associated with malignant disease of the gall-bladder, might furnish more than a clinical hint relative the nature of the ailment and might also throw considerable light, etiologically, upon the relationship existing between chronic gall-bladder irritations (infective chemical, foreign body: *e. g.*, calculi) and gall-bladder irritation. It should be here emphasized that chonicity, histologically speaking, must be differentiated from chronicity indicating months or years duration of disease; a powerful, continuously-acting stimulus may be quite capable of producing histologic changes of malignancy quite as marked as those occurring where an intermittently acting or weakened agent has been manifest over a long period of time.

(*a*) *Symptomatology.*—In 17 patients the early history of the affection indicated rare or frequent attacks of such dyspepsia as is commonly associated with catarrhal cholecystitis or cholelithiasis. Not rarely, these attacks had borne definite relationship to an acute infectious disease. The history of typhoid fever was obtained from 12 patients, pneumonia from 3 and malaria from 1. At the time of their coming to the hospital, in 20 instances the patients were affected with a continuous and disabling ailment. The characteristics of this ailment now will be considered.

(*b*) *Appetite.*—In 14 patients (60.8 per cent.) there was

persistent anorexia. The food desire was lessened in 5, but well maintained and in no wise abnormal in 4.

(*c*) *Weight Loss.*—There was but one patient who had maintained normal weight. In this case early exploration to relieve distressing gall-bladder dyspepsia disclosed early sessile papilloma. In the remaining 22 cases of my series weight loss, generally associated with physical weakness, averaged 28 pounds (minimum 15 pounds, maximum 60 pounds). The weight loss was frequently astonishingly rapid and of itself, when taken in connection with an ailment clinically dependent upon gall-bladder malfunction, should have furnished a significant hint relative to the development of neoplasm. In three months one patient lost 40 pounds, another 60 pounds, in seven months, and a third 28 pounds in five weeks. It was not unusual for persistent weight loss associated with unaccountable anorexia weakness or diarrhea to cause alarm a considerable time before symptoms or signs of gall-bladder anomaly presented. Five patients came for the examination at which malignancy was discovered on account of the persistent and puzzling loss of weight.

(*d*) *Bowels.*—In 11 cases distressing constipation was recorded; in 4 stools of normal frequency, while 8 patients were subject to diarrhea, not rarely uncontrolled by diet and commonly exhausting. Nocturnal diarrhea, with disturbance of sleep and rest, seemed to be an important influence in causing rapid weight loss and cachexia. This was especially noticeable where the gall-bladder malignancy had invaded the pancreas (6 cases).

(*e*) *Stools.*—There were no abnormal findings in 8 instances. the stools of the remaining 15 patients persistently or intermittently indicated interference with free bile flow. They were definitely acholic in 9 cases.

(*f*) *Bile Pigment in the Urine.*—As shown grossly by dark colored urine, capped with thick green-brown or olive froth or by chemical test was present in 11 instances. The urine analyses of 5 patients returned report "suspicious" for bile coloring.

(*g*) *Jaundice.*—This was definitely manifested by 14 patients. In three patients the jaundice was intermittently present. In 11 patients the jaundice was persistent. In these cases the skin coloration and the sclerotic tinting ranged from lively greenish-brown to a muddy or dusky olive green. Itching of the skin or distressing anal pruritis was obstinate in 7 of the continuously

jaundiced patients. Such itching was often of significant importance with respect loss of sleep and rapidly developing weakness.

(*h*) *Fever.*—Although Musser concludes that in malignancy of the gall-bladder the temperature is apt to be subnormal, rise in temperature, with or without chilly sensations or sweats, was recorded in five patients of my series. Its character was similar to that of cachectic processes associated with malignancy in general or with such exhausting ailment as progressive tuberculosis, *viz.*—a subnormal morning temperature with a rise towards evening or upon unwonted physical or mental exertion. The maximum temperature recorded was 102.3. In one instance of indefinite upper abdominal nodular tumor, not associated with jaundice or pain, the character and persistence of the fever led to a pre-operative diagnosis of tuberculosis of the peritoneum. In the presence of ascites such mistake in diagnosis is not easily avoided unless there be careful scrutiny of the patient's history previous to the period of his presenting complaint.

(*i*) *Pain.*—Some degree of abdominal discomfort was experienced by 21 patients (91.2 per cent.). There was severe pain in 16 cases (69 per cent.). In 5 cases sharp, prostating colic-like attacks of pain required opiate relief. In 2 patients the character of the pain suggested gall-bladder perforation.

The abdominal distress was *continuous* in 14 cases, but only *intermittently* manifested in 7. It was not unusual to note aggravations of pain, even of colic-like degree, in those patients where a continuous abdominal discomfort had been experienced.

(*j*) *Location of Distress.*—Eleven patients complained of general epigastric pain; in 5 discomfort was definitely confined to the right upper abdominal quadrant, in 1 each distress at the right costal arch, the region of the navel and the xyphoid. In 2 instances there was generalized liver region pain with a point of intensity below the tip of the right scapula.

(*k*) *Transmission of Pain.*—There was persistently referred pain in 14 cases. In the order of frequency, pain transmission occurred to the right back, the right shoulder, the tenth to twelfth dorsal vertebrae and the mid-epigastrium. Distress at the referred point was not infrequently more annoying than was that experienced at the zone of pain inception.

(*l*) *Time of Pain.*—Maximum distress was commonly re-

corded as occurring shortly after the taking of food upon sudden changes of position or after jolting or jarring (*e. g.*, after a ride over a rough road). Only two patients complained of severe night pains.

(*m*) *Relief of Pain.*—In 8 instances opiates were required to make the patient comfortable. Fasting, vomiting, free catharsis, gastric lavage or the administration of alkalies were commonly helpful agents.

(*n*) *Abdominal Tenderness.*—This was recorded in 22 of the 23 cases. It was usually in the right upper quadrant or in the epigastrium generally. In 7 instances the tenderness was so exquisite as to suggest gall-bladder perforation with protected peritonitis.

(*o*) *Abdominal Tumor.*—Such was definitely determined or indefinitely delimited in 17 cases (74 per cent.). The tumor or ridge commonly occupied the right upper abdomen. In 4 cases it extended well across the epigastrium. In size the tumor ranged from a finger-like ridge to an oval or pear-shaped mass as large as a grapefruit. Its *consistency* was commonly firm, although in 3 instances there was a cystic feel with a suggestion of fluctuation. Its *surface* was definitely rough or nodular in 9 cases. The tumor was *movable* on respiration or change of position in 4 instances. In the remainder the mass seemed deeply fixed. *Tenderness* over the tumor was noted in 12 patients.

(*p*) *Enlargement of the Liver.*—Occurred in 11 patients (46 per cent.) of the entire series and in 8 cases (47 per cent.) where abdominal tumor was coincident. In degree the liver enlargement ranged from the organ's being just palpable to its extension downward as much as 5½ inches below the right costal limit. Of the 11 patients in whom the liver was enlarged there was palpable hepatic nodulation in 4. The liver consistency was commonly very firm, in fact, so firm as to suggest the diagnosis of interstitial cirrhosis. Two patients were brought under observation with such previous diagnosis. In one case there was concomitant splenic enlargement.

(*q*) *Ascites.*—This was demonstrated in 3 patients (13 per cent.) before laparotomy. In other patients free abdominal transudate was discovered at operation (ascites, 21.7 per cent. for the series). Pressure upon or actual malignant invasion of the portal vein or its radicles commonly produced the ascites. In

one instance there was involvement of the receptaculum chyli and the thoracic duct with a resultant chylous ascites.

(*r*) *Belching and Nausea* were annoying in 17 patients. With these symptoms a distressing sensation of upper abdominal "crowding" or "up pressure," particularly at night or after eating was sufficiently uncomfortable to prevent adequate feeding or uninterrupted sleep.

(*s*) *Vomiting.*—This occurred either as a daily or an irregular event in 18 patients (79 per cent.). Vomiting of retained food was observed in 10 patients. The vomitus of 13 patients was persistently bile stained. In 3 cases where obstruction occurred near the papilla of Vater the vomitus was persistently colored with muddy brown bile. In these cases the gastric extracts prossly suggested those commonly to extensive malignant stenosis of the pyloric end of the stomach.

(*t*) *Test Meals.*—Data is available in 12 cases. Persistent 12-hour food retention existed in 5 cases. The *average free HCl* was 21 (minimum 4, maximum 56). There were 6 instances of achlorhydria. The *average total acidity* was 30.1 (minimum 4, maximum 64). *Chemical test* for blood pigment was positive in the gastric extracts from 6 patients. *Lactic acid* was recorded in 5 cases.

Microscopically.—Yeasts were in excess in 5 cases and sarcines coincident in 4. Organism of the *Boas Oppler* type were present in 3 of the achlorhydria gastric contents where there was associated food stagnation.

(*u*) *Roentgen Findings.*—There were 11 cases where Roentgen examination had been made before laparotomy. In 5 cases X-ray plates demonstrated atypical shadows in the gall-bladder zone strongly suspicious for calculi. In 3 cases there was interference with the emptying of the stomach, the barium meal remaining longer that six hours in the gastric cavity. In one case there was a filling defect at the outlet of the stomach which interpreted in the light of the clinical symptomatology and the test meal examination appeared to result from pyloric cancer. At fluoroscopy the Roentgen examination not rarely proved of service in demonstrating that at the palpable abdominal tumor lay outside the stomach or other portions of the alimentary tract. There was one instance where the malignant gall-bladder involved the hepatic flexure of the colon. In this case there was not only

a colon filling defect, but also marked retardation in the progress of colon contents caudad.

(*v*) *Operative Findings.*—1. *The Neoplasm.*—In 4 cases the malignant change was well defined and located in the fundus or body of the gall-bladder. In two cases there were malignant papillomata. In the remaining 17 cases there was extensive neoplastic involvement of the entire gall-bladder with contiguous invasion of adjacent viscera.

2. *Histologically,* the lesion was constantly carcinoma of the columnar or spheroidal cell type.

3. *Concomitant Incidence of Gall-Stones.*—Of the 26 instances of primary malignancy of the gall-bladder cholelithiasis was an associate finding in 16 patients (69 per cent.). In the remaining 7 patients it was not possible to prove the previous presence of gall-stones, although in 4 cases the early histories suggested such. The relationship of cholelithiasis to malignant disease has already been commented upon. It would appear that the fact that gall-stones are often found in malignant gall-bladder furnishes evidence worthy of note with respect to gall-stones acting as sources of irritation and the production of malignant hyperplasia of the gall-bladder mucosa. It is not impossible, however, that in malignant gall-bladder calculi may form as a consequence of cancerous change altering the excretory function of the gall-bladder mucosa or preventing proper emptying of the viscus. From the clinical histories of many patients who later on are shown to have malignant disease of the gall-bladder, attacks simulating gall-stones can be elicited at a time previous to the more recent ailment, which is apparently clinically malignant. It would certainly seem that in patients in whom gall-stones can be proved to exist, from the clinical or special examinations, their early removal, together with the gall-bladder, might be a considerable factor in preventing malignancy in the individual and also in the human family.

4. *Involvement of Adjacent Viscera.*—In 11 cases the lymph-nodes showed metastases; in 8 cases the liver was extensively invaded; in 6 the pancreas; in 2 the stomach, and in 1 case each there was extension to the omentum, the hepatic flexure of the colon and the retroperitoneal lymph tissue.

(*w*) *Operative Procedure.*—In 11 patients abdominal exploration only was possible on account of extensive malignancy. In

4 cases cholecystectomy was performed and once posterior gastroenterostomy for the relief of pyloric obstruction. In the remaining 7 patients the gall-bladder was drained.

(*x*) *Result.*—Two patients recovered and have remained well longer than four years. Total termination followed in the remainder either shortly after operation or within eight months subsequent to leaving the hospital.

(*y*) *Conclusions.*—

DISCUSSIONS.

Dr. David Riesman, Philadelphia, Pa.: The loss of weight to which Dr. Smithies has referred may occur in cases of jaundice that are not due to malignant disease. I have seen profound emaciation in long continued jaundice, in which operation or subsequent development proved that the case was not one of carcinoma. I remember a man who had lost fifty pounds in weight. He was about fifty-five years of age; was deeply jaundiced; everything in the case pointed to a growth, though none could be detected on physical examination. At operation nothing was found except an obstruction to the common duct by gritty material. The duct was cleaned out, the gall bladder drained; the man made a complete recovery. It may be that the emaciation in non-malignant cases is due to loss of appetite and the loss of sleep often caused by itching.

Dr. Martin E. Rehfuss, Philadelphia, Pa.: I have been struck by this paper of Dr. Smithies, which is splendid. I have been engaged on the problem of pancreatitis lately, and have a number of cases resembling those which Dr. Smithies has mentioned. The interesting thing is this very question that Dr. Riesman has brought up. I have collected, in two years, six cases of chronic pancreatitis operated on, in which the weight loss was tremendous. In fact, the thing that impressed me most with it was the tremendous weight loss, coupled with a blood count that was low. The patients developed cachexia, and the lowered blood did not develop coincidentally. A patient operated on by Dr. Dacosta had anorexia, achlorhydria, and traces of blood in the stomach, and the gall bladder was drained. No stone was found, but drainage was carried out to get rid of possible coincident infection. I have followed the case for the last year, and was called in to see it again. The man had regained a great deal of his lost weight. This is contrary to the cases that I have seen. I find that they are the most rebellious cases, next to malignant ones. I have tried enforced feeding, with but little relief. The patient has gained thirty (?) pounds.

Another individual, operated on by Dr. Stewart, lost fifty-five or fifty-six pounds. Both were benign affections of the pancreas. Both patients are living, and both have gained in weight since the operation. This case, which Dr. Brown has seen, and which I am seeing

at present, is one of those difficult cases. There is blood in the stomach, with achlorhydria and a tumor, and the tumor is in the region of the gall bladder. Dr. Brown's diagnosis is primary carcinoma of the gall bladder. My diagnosis is that there is a tumor at the head of the pancreas.

Examination of the stomach fails to reveal any condition whatever. This shows how difficult these cases are.

I should like to ask Dr. Smithies one more question, because I have discussed it with surgeons, and particularly Dr. Deaver, who could not answer it. It is a little apart from the subject now under discussion, however. It is this: Does cholecystectomy, removal of the gall bladder, or does drainage of the gall bladder, cure infection. We have been culturing the bile. I have seen recently a number of cases —three, in the last two months—operated on, and still with symptoms of infection. Two of these have persistent tenderness and infection, and in one case, there is a rise in temperature. I should like to know what Dr. Smithies has to say in regard to this matter, because the appalling number of cases he mentioned places him beyond the general average of observers. I do not know of anyone else who has seen twenty-three cases of carcinoma of the gall bladder.

Dr. Frank Smithies, Chicago, Ill., closing: It was very kind of the members to discuss the paper so late in the session, particularly a paper so full of figures.

Answering Dr. Rehfuss's question, first, I would say that I believe that cholecystectomy or cholecystotomy will frequently leave a case with infection, because the infection has often got out into the lymph-nodes far removed from the gall bladder.

Dr. Rehfuss: I mean from a general surgical standpoint, aside from that.

Dr. Smithies: In my own case, I should have my gall bladder taken out. The drainage gives relief, because it has been shown in a great number of cases that the most active infection is in the fundus of the gall bladder. The drainage operation destroys that portion or the resultant scar mechanically blocks the lymphatics and nature then takes care of the infection.

Regarding the incidence of malignancy, which Dr. Rehfuss mentioned, it has been my experience that in all these anomalous conditions, it is a good plan to examine blood serum for evidences of lues; certainly should the case appear hopeless from a surgical standpoint. Specific treatment not rarely aids particularly when there exists an anomalous lesion of the pancreas. We had a young doctor, a year and a half since, who had four operations for a large tumor of the head of the pancreas and it proved to be a gumma.

With respect to the blood in achlorhydric cases, I would say that blood is not an infrequent finding in the stomach contents in cases of achlorhydria. The wall of the stomach is easily traumatized by mechanical, chemical or bacterial agents.

Dr. Draper's question is hardly within the scope of this paper, because I stated that in this series there were no incidences of carcinoma of the bile ducts or bile passages, but that these were cases of carcinoma of the gall bladder.

Dr. Riesman's point is well taken, because it is the common opinion that it is very easy to diagnose carcinoma of the gall bladder. Mayo makes that statement. We only made thirty per cent. of absolutely correct prelaparotomy diagnoses. Of course, one may string out everything he thinks of on a history card, and then say that correct diagnosis was made, but our records show only thirty per cent., so that Dr. Riesman's point of loss of weight occurring in obstruction of the ducts is well taken. I think that this thirty per cent. represents a good average of frequency of correct prelaparotomy diagnosis of cancer of the gall bladder. But the best part of my diagnosis in these cases is that I give the patients the benefit of the doubt and insisted on a surgical exploration. Such exploration often revealed a condition that was not malignant and could be cured and in the cases of papilloma removal of the gall bladder was possible and in such event the malignancy cured.

DR. LICHTY: The paper of Dr. Smithies is now open for discussion.

DR. JOHN W. DRAPER, New York City: It seems to me as though this were the best contribution that I have heard on this subject for a very long time. I should like to ask Dr. Smithies whether he made any notes in this study on the incidence of malignancy at the ampulla. I noticed that he said, or I understood him to have said, that there were no instances of malignancy in the bile ducts themselves. I have been very much interested in the absence of malignancy in the first portion of the duodenum, and I had always believed that it occurred at the ampulla.

DR. JOHN BRYANT, Boston, Mass.: I should like to ask a question. Is there any possibility that these destructive bacteria may be used therapeutically for the removal of gall stones?

PHYSIOLOGIC CONSIDERATIONS IN THE IMMEDIATE TREATMENT OF DANGEROUS HEMATEMESIS.

By W. A. Bastedo, M. D.,

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1. *The Condition of the Circulation.*—In hemorrhage the fall in arterial pressure from great loss of blood volume is counteracted as far as possible by certain reactions in the body, the chief of which is the contraction of the peripheral arterioles, the result of stimulation of the vasoconstrictor center. This contraction is a gradually increasing one as the hemorrhage progresses (Wiggers), except that at a late stage there is paralysis of the vasoconstrictor center with general vasodilation (Pilcher and Sollmann). As the cerebral and the cardiac coronary arteries are not under the control of the vasoconstrictor center, the general peripheral constriction does not include them, and consequently there is a greater flow of blood through these unconstricted arteries, a provision in nature to maintain the efficiency of the vital organs, the brain and the heart. Indeed, the coronaries, at least, not only do not contract but may even dilate; for it has been shown by Wiggers that after hemorrhage the coronary flow equals or exceeds the normal flow, even though the systemic arterial pressure is below normal.

The heart, therefore, does not suffer so much as other organs, and as shown by cardiographic tracings, maintains its normal contractile power even after considerable loss of blood (Wiggers). There is, therefore, ordinarily no reason for giving strophanthin or digitalis or any other drug to maintain the heart; and there is contraindication to any drug, such as nitroglycerin, to overcome the general peripheral constriction, which is not only a necessity for the maintenance of the blood supply to the heart and the vital centers of the brain, but may be, in addition, the means of shutting off the bleeding vessel itself.

Read at the annual meeting of the American Gastro-Enterological Association, Atlantic City, May 7, 1918.

2. *The Limit to Hemorrhage.*—Of much greater importance than the total amount of blood lost is the rate of loss, a sudden loss being a more serious matter than a gradual depletion to the same degree. But even with rapidity much blood must flow before the patient is in real danger. Experimental work indicates that it requires a rapid loss of from 4.5 to 5.5 per cent. of the body weight of a normal dog to cause death (Levin), and if we apply the minimum of these figures to man it would mean that the fatal point is not reached in a man of 150 pounds till he has rapidly lost 6¾ lbs. of blood, or about 6⅓ pints. That this is correct for the human being has been shown by Gjestland, for in statistics bearing on the power of the human to lose blood and yet recover, he reports the cases of two women with postpartum hemorrhage who each lost about 3,000 gm. (6⅔ pounds) of blood and recovered, one woman being discharged from the hospital on the fifteenth day and the other on the twenty-seventh. If an illness antedates the hemorrhage, as in the case of cancer, chronic ulcer or cirrhosis of the liver, the fatal amount will, of course, be less, according to the extent and character of such preceding illness. But if the hemorrhage recur at several hours interval the total fatal amount will be more, for the blood volume tends to be restored by absorption of tissue fluid, and the blood-making organs rapidly furnish a supply of blood cells.

3. *The Cessation of Bleeding.*—The natural process by which hemorrhage is checked is the obliteration of the opening in the bleeding vessel. In some cases this is favored by the retraction of the vessel, but in all cases it requires the formation and retention of a clot at the opening. The clot, however, because of the force of the blood flow, does not form at once at the opening in the vessel, but beginning at some distance away, reaches back by accretion till it covers the opening; then it stops the bleeding. The distance at which the clot thus begins to form is determined by the force of the blood ejection and the degree to which the blood is held of the blood ejection and the degree to which the blood is held in contact with the injured tissues; therefore, as the stomach is a hollow viscus it may permit a great deal of blood to spurt out into its lumen before any of the blood succeeds in clotting and clinging to the tissues in the immediate neighborhood of the lesion. This is one reason for the frequency of large hemorrhages

from the stomach. Hence, in the treatment it is desirable to ensure *contraction of the stomach,* a state which not only tends to permit the bleeding vessel to retract instead of remaining on the stretch as in a distended organ, but also, because of the larger and more closely packed folds of mucous membrane, may result in a retarded flow of blood.

In these cases of bleeding there is, as a rule, no thrombosis in the lumen of the vessel until some time after the opening of the vessel has been sealed. Hence, the surface clot may at first be easily loosened, and if loosened permits resumption of the bleeding. Other factors which may interfere with the formation of the clot or may cause a clot to break loose are: 1. Active peristalsis; 2. Undue temporary increase of blood pressure such as may result from the accelerated respiration and increased heart-rate; 3. Sudden accesses of blood-pressure such as may be brought about by vomiting and by large and rapid intravenous administrations of fluid, and 4. Mechanical interference, as by injudicious lavage.

To favor and maintain effective clot formation we need, therefore, *a quiet contracted stomach, quiet heart and quiet respiration, avoidance of vomiting, and careful watching during the introduction of fluids to restore the blood volume.* The acceleration of the heart and respiration are due not only to direct depression of the vagus center and direct stimulation of the respiratory center, but also to the reflex effects of general nervousness and anxiety. The best remedy for these is a hypodermic of *morphine,* which through its effects upon the respiratory and vagus centers slows the respiration and the heart, and by its action on the cerebrum lessens anxiety and nervousness. It also depresses or abolishes peristalsis, and by central action lessens the tendency to vomiting. These are very great advantages. But morphine has the striking disadvantage that, while is abolishes peristalsis, it also abolishes tone in the stomach wall, so that in large doses it produces an atonic dilatation, a state just the opposite of that desired. To counteract this I would accompany the morphine with a maximum dose of strychnine, for strychnine acts to promote tone in the stomach muscles and thus opposes the morphine disadvantage without appreciably counteracting the desired effects of morphine on the respiratory center, the vagus and the cerebrum. Contrary to a prevalent belief, strychnine does not activate the circulation.

Atropine has been employed to counteract the effects of morphine on the stomach, and it does this to some degree; but in the large doses necessary it also annuls the desirable control of the vagus over the heart.

Lavage.—If the stomach remains distended and if there is evidence that the bleeding still continues, *i. e.,* that an efficient clot has not formed, lavage, in my opinion, may properly be employed. If the bleeding seems to have stopped or if the patient gags severely on the introduction of the tube, lavage should not be employed. Lavage should, of course, be carefully done, the amount of added fluid being rather small. That there is an advantage in the use of excessively hot or excessively cold water is rather doubtful, for such liquids are prone to set up peristalsis. The use of the tube has an added advantage in that it permits the introduction of a coagulant after the stomach is washed out, an ideal time for it to come in contact with the bleeding tissues.

Emetine has been employed to stop the hemorrhage, but its pharmacologic action shows that there is no justification for its use for such a purpose. It is a depressant of the vasoconstrictor center (Sollmann), and at once or following a transient vasoconstriction it produces definite vaso-dilation (Pellini and Wallace). Furthermore, Howell states that it retards clotting by causing a deficiency in the fibrinogen of the blood.

4. *Venous Hemorrhage.*—As the venous system of the stomach empties normally into the portal vein, and the average mean portal blood pressure is only 10 mm. of mercury (Starling), a venous hemorrhage from erosion due to a stomach lesion is without great force and usually quickly ceases. Therefore, except in the rare cases of perforation of a very large vein, such as the portal, splenic or superior mesenteric, venous hemorrhage from an ulcer or cancer is probably never great. However, in the cases with portal congestion, as in portal thrombosis or cirrhosis of the liver, the portal venous pressure is much higher than this, and consequently venous bleeding is more vigorous and more prolonged. But even then the bleeding ceases as soon as the portal congestion disappears, and in all but exceptional cases is prone to be beneficial to the patient rather than harmful.

But in just these cases of portal congestion a serious venous hemorrhage with which we may have to deal is that from the submucous veins of the lower third of the esophagus. At one

end these connect with the coronary veins of the stomach and at the other end with the systemic venous system, so that they form a free communication between the portal and systemic veins. In portal obstruction they undergo a compensatory dilatation (Quain) with a marked tendency to become prominent in the esophageal wall and to form varices. (See Fig.) Thus they are subject to traumatism or to spontaneous rupture, and when ruptured are a source of hemorrhage from both the portal and the systemic venous systems. Furthermore, owing to the comparative smoothness of the esophageal mucous membrane the blood finds no hindrance to its flow and little tissue to clot upon and cling to. Moreover, as shown by Whipple and Hurwitz, in cases of hepatic cirrhosis there is a marked diminution in the fibrinogen content of the blood and consequent retardation and imperfection in the clotting; or as stated by Clowes and Busch, "even in the presence of an adequate proportion of thrombin the clot formed is not sufficiently tough to effect the desired result." Hence these hemorrhages, though venous, may be large, and are occasionally fatal. As the blood is brought up by vomiting, they are not usually distinguished with certainty from gastric hemorrhages; and as the passage of a stomach tube would be dangerous, it should be the rule that *in gastric hemorrhage if there is evidence of portal congestion lavage is absolutely contraindicated.*

5. *Measures to Retard the Ejection of the Blood.*—For this purpose the substances in use are the local vaso-constrictors, such as epinephrine, and materials of colloid nature to increase viscosity.

Epinephrine (adrenaline) acts locally to constrict the bleeding vessel and so to retard the flow of blood and permit clotting. It is administered by mouth in amounts of 4 to 15 cc. (1 dram to 1 ounce) of the 1 in 1000 solution of the hydrochloride, diluted with about 2 to 5 times as much water to make bulk enough to coat the stomach. It has the disadvantage that it tends to induce strong peristalsis. The same may be said of pituitary. Though, when administered intravenously, epinephrine distinctly increases the coagubility of the blood (Cannon and Gray) by increasing the prothrombin (Crabfield), and in the general splanchnic constriction may constrict the bleeding vessel itself, yet it cannot safely be used intravenously because of its marked effect in heightening the systemic blood-pressure.

The Colloid Materials in use are gelatin and acacia, which on injection intravenously or, perhaps, subcutaneously, tend to increase the blood's viscosity and so to act mechanically to retard the escaping blood. We shall speak of these later.

6. *Measures to Increase the Blood Coagulability.*—Besides the actions spoken of above, there is a natural progressive increase of the blood's coagulability as hemorrhage continues (Drinker and Drinker, Gray and Lunt). Indeed, so strikingly does hemorrhage tend to cease at the point of syncope, that Crile has advised a return to the method of the older physicians who would sit the patient up and perform venesection to hasten the onset of syncope. J. Kaufmann reports seeing Kussmaul successfully carry out this principle in a case of extreme hemoptysis.

If by the natural processes adequate clotting fails to occur we may attempt to supply an agent that will hasten the formation of the clot. Accepting Howell's terminology for the sake of uniformity, the clotting elements in the plasma of the circulating blood are: prothrombin, calcium and fibrinogen, and in addition some thrombin; the anti-clotting elements are antiprothrombin and antithrombin. In clotting the prothrombin is liberated, and, taking up calcium, changes to thrombin; and this free thrombin quickly precipitates the fibrinogen in the form of fibrin, *i. e.*, it produces clotting. In the intact vessels clotting is prevented by the anticlotting elements, which hold the prothrombin and thrombin in neutral combination. Normally there is a great excess of anticoagulent in the blood, so that much prothrombin and even thrombin may be added to the circulating blood without thrombosis resulting (Davis). In hemorrhage the disintegrating blood platelets and leucocytes and the tissue juices of the injured tissues supply the lipoid thromboplastin (cephalin, cytozyme, thrombokinase); and this has such an affinity for the anticoagulants that it breaks up the prothrombin combination and sets free the prothrombin to take up the calcium and coagulate the fibrinogen, and so form the clot.

In profuse hematemesis there is no reason to suspect a deficiency in any of the coagulation elements of the blood; but owing to the rapid passage of the blood beyond the injured tissues, as in a hollow viscus like the stomach or esophagus, there are cases in which the prothrombin is not liberated quickly enough to form a clot at a point sufficiently close to the bleeding vessel

to bring about cessation of the bleeding. The clotting takes place at the normal rate, yet not quickly enough to be of use where it is wanted. Therefore we think of the possibility of employing agents to favor clotting, even though, on testing, the coagulation time of the blood proves to be normal. For this purpose there are several substances for use both locally and systemically. They may be called *Coagulants,* and the principal ones in use are: 1. Cephalin or thromboplastin; 2. Extracts of the blood-platelets; 3. Blood serum, the serum derivatives euglobulin and coagulose, and defibrinated blood, and 4. Whole blood.

The increase of coagulability through the local application of one of these coagulants can readily be comprehended; though it requires that the remedy be kept in contact with the bleeding tissue for several minutes. But the cessation of bleeding after the intravenous or even subcutaneous injection of a small amount of a coagulant is less well understood. Doubtless the administered element, if it acts at all, does so by changing the relations between the clotting and anticlotting elements present in the blood, and it may do this either by supplying a coagulative element, such as prothrombin, by supplying substances to neutralize the anticoagulant elements, or by exerting some activating effect upon the blood-forming tissues. The coagulants can hardly be of use to check an immediate profuse hemorrhage, but they may be of value in a continuous small hemorrhage or in preventing a recurrence of profuse hemorrhage. The dose of any coagulant needs to be repeated frequently as its action is short-lived.

Cephlin or Thromboplastin acts by taking up the antiprothrombin and antithrombin and setting free the needed prothrombin and thrombin. It is marketed under the titles Thromboplastin-Hess and Kephalin. They both contain the physiologic lipoid cephalin or thromboplastin, and both are prepared from brain tissue, though by different processes. *Thromboplastin-Hess* is a solution in Ringer's solution of tissue juice from the brain with a fine suspension of brain tissue. It is preserved by 0.3 per cent. of trikresol, and may be sterilized by boiling. Hess verbally recommended to me a dose by mouth of 4 cc. (℥i) in 15 cc. (℥ss) of water every half hour for three or four doses, but the manufacturers recommend 20 cc. (℥v) diluted 12 to 15 times with water. Dilution does not affect its coagulating power. It has been given in amounts up to 60 cc. (℥ij) in a day without any

toxic effects. It is also used subcutaneously or intramuscularly in amounts of 10 c.c. (℥iiss) at a time. The subcutaneous dose is painful. *Kephalin* is an ether-acetone-alcohol extract of brain evaporated till the yellow fatty or lipoid residue remains. It is not destroyed by boiling. For use by mouth or intramuscular injection its dose is 10 to 30 drops in physiologic saline repeated every 6 to 12 hours. It corresponds in action with thromboplastin-Hess. It seems to be rapidly absorbed from the alimentary tract, for Howell found that a solution given by mouth showed a lessening of the coagulation time in as short a period as forty minutes.

Kephalin and Thromboplastin have also been introduced intravenously, but as they supply the material to produce coagulation of the blood, and so have a tendency to bring about thrombosis in the vessels, the procedure is a dangerous one. In 1 per cent. solution Mannheimer and Wang employed Thromboplastin-Hess intravenously in tuberculous hemoptysis in twenty-two instances and noted no apparent benefit from any dose. In undiluted form Wang injected 5 cc. into the ear vein of a rabbit and the animal died almost immediately with a firm clot in the veins of the neck and in the right auricle extending to the ventricle. Hess gave an intravenous of 2 cc (℥ss) of a 10 per cent. solution to a rabbit and shortened the coagulation time by one-half, though there was no clotting in the body. In dogs, Howell found that an intravascular injection of Kephalin, 0.1 gm. per kilo, shortened the coagulation time from one-third to one-half without any intravascular clotting, the eeffct lasting for at least one or two hours. Apparently, therefore, a weak solution intravenously is of no use, and a strong solution is not without danger, at least, for any one but hemophiliacs, who have an excess of anti-coagulants in the blood. It is a question, then, whether any amount that would be effective could be used without danger. I have the word of Dr. Hess that the substance should not be used intravenously.

Coagulen is a powder prepared from blood-platelets by fractioned centrifuging, followed by desiccation and dilution with lactose. It is claimed that it is a preparation of lipoid material and that 1 gram (gr. xv) of the powder represents 20 gm. (℥v) of dried blood. It is readily soluble in water and may be sterilized by boiling. According to Howell, the platelets of blood

yield both prothrombin and thromboplastin, and the action of coagulen is that of thromboplastin. In gastric hemorrhage the local action may be obtained by the administration of 20 to 60 cc. (3v-xv) of a 10 per cent. solution by mouth. Fonio, its introducer, recommends 50 to 75 c.c. (1⅔ to 2½ oz.) of a 3.5 per cent. solution intravenously and a similar amount subcutaneously, stating that the subcutaneous injection of a stronger solution is painful. From the intravenous use there is the same danger as in the case of thromboplastin.

Blood-serum.—This is plasma from which have been removed not only the blood cells, but also the coagulative elements of the clot. It has therefore lost part of its power to induce clotting. It contains prothrombin and thrombin in combination with antithrombin, but it lacks fibrinogen. The prothrombin is intimately associated with its euglobulin fraction. Serum is not a powerful coagulant, and does not cause intravascular clotting even when amounts of 200 cc. or more are introduced intravenously. Yet in some cases it seems to have a value out of proportion to its coagulative power, even when employed subcutaneously, so that it has been considered by some an activating agent, stimulating the production of clot-forming elements. It has the great disadvantage that it contains 6 to 7 per cent, of proteins, and thus unless of human origin exposes the patient to anaphylaxis. It also rapidly deteriorates so that after fifteen days it has lost seriously in potency; therefore fresh serums as from the human being, rabbit, sheep and horse are preferable to stock serums. Ox and dog serums are too toxic to human beings to admit of their employment. According to Clowes and Busch, human serum is in no wise superior in clotting power to that of the animals mentioned, yet it is preferred because, being homologous, it may be used in much larger quantities with safety. Lee and Vincent state that rabbit's serum is the most potent readily available serum. Rettger thought that the loss of ability of serum to produce coagulation was due to a slowly formed, loose combination of the thrombin with the other constituents, and stated that serum that had lost its potency could be reactivated by the addition of weak alkalies or acids with subsequent neutralization. Howell has confirmed this finding.

The dose of the animal serums intravenously is 100 cc., and subcutaneously 10 to 50 cc, every 6 to 12 hours. But of fresh

human serum I have heard Dr. Willy Meyer say that he has repeatedly injected subcutaneously 400 or 500 cc., and Judd has reported the use of 180 cc. of the mother's serum in the case of a baby. It takes two to twelve hours to obtain the separated serum from fresh blood, and, according to Hess 12 to 24 hours for the subcutaneous dose of a serum to influence clotting.

For want of available serum diphtheria antitoxin has been employed, and in the past has been found useful; but the refined and concentrated antitoxin at present used contains a very high percentage of protein, about 16 per cent., and this almost entirely pseudoglobulins which have almost no value as coagulants (Hess).

Euglobulin.—On account of the high protein in serum, and its rapid deterioration as a coagulant, Hess separated the proteins and found euglobulin to be the important coagulative element. As euglobulin is only about ⅓ of the total protein, a solution of it of the same strength as in the serum represents almost the total coagulative power of the serum with only ⅓ the percentage of protein. It thus gives a lessened chance of severe anaphylaxis. Hess passes it through a Berkefeld filter for sterilization and adds 0.3 per cent. of trikresol as a preservative. But it does not long retain its potency, and is not at present marketed.

Coagulose is a precipitate obtained by treating horse serum with a mixture of acetone and ether. It has the coagulative properties of horse serum, and retains its potency for a long time. It is prepared aseptically, and is kept dry in sealed glass bulbs containing 0.65 gm. (gr. x) of the powder. It is made ready for use by the addition of 8 cc. of sterile water, the temperature of which is not above 40 degrees C. This amount representing 10 c.c. of serum may be employed subcutaneously, intramuscularly of intravenously. To make a satisfactory solution it should be dissolved by rotation of the bulb without shaking.

Blood serum and these derivatives lose their coagulative power when heated to a temperature of 60 to 70 degrees C., therefore cannot be sterilized by heat.

Defibrinated Blood.—The defibrination removes fibrinogen and blood platelets, but Ottenberg and Libman state that in the process of defibrinating the blood cells are mechanically injured to some degree, so that their products are present in the defibrinated blood and if the introduced amount is large may cause intravenous clotting.

Whole Blood.—The treatment of internal hemorrhage by the intramuscular or subcutaneous injection of whole blood in small amounts has recently been recommended (Curtis, Emsheimer, Howard), even amounts as small as 10 c.c. being employed. It would seem to us to have no value above that of serum, except that it may be used at once, while it practically forms a hematoma in the tissue with the usual slow absorption of the clotted blood. *Calcium* as a coagulant is futile in these cases, for to affect the coagulability of the blood it must be given in huge doses for many days. (For discussion see the author's Materia Medica, Pharmacology and Therapeutics, 2nd Ed., 1918.)

Styptics.—The local use of the chemical styptics, such as tannic acid, ferric chloride, Monsel's solution and alum, should be condemned, as they are irritant and tend to cause excessive peristalsis, nausea and vomiting.

7. *Measures to Restore the Blood Volume.*—In case the hemorrhage does not cease, the volume of the blood is soon reduced so low that the mechanical functions of the circulation cannot be carried on. It is then necessary to add fluid to the circulating blood.

Transfusion.—We have more faith in the transfusion of blood than in any other single measure, or in all the other measures put together, for it tends to fill the vessels with a liquid of the same physiologic nature as that which has been lost, it prevents the lowering of viscosity which would otherwise take place whether the result of hemorrhage or of added saline, and it is not readily lost from the vessels by osmosis. For the transfusion I should prefer the syringe-canula method of Lindemann or of Unger, for the sodium citrate method (Weil, Lewisohn) and the hirudin method (Satterlee and Hooker) involve the introduction of a substance that prevents clotting, and this would seem to be undesirable in a bleeding patient already much depleted of blood. However, in the use of sodium citrate this factor has proven to be a small one, so that if it is the only method available it may be employed. In using the citrate method I should recommend a strength of 0.25 per cent. of sodium citrate, as we have had clotting occur with the 0.20 per cent. strength recommended by Lewisohn. There are many reported instances in which the bleeding ceased quite promptly following or during transfusion. On the other hand, there are cases in which bleed-

ing seemed to recur because of the transfusion, and I might repeat the caution that if the bleeding has stopped the blood pressure should be watched during the transfusion lest the clot be loosened by an access of pressure.

In severe hemorrhage Bernheim's rule is that transfusion should be performed if the systolic pressure drops to 70; and he affirms that the seriousness of the loss is not to be estimated by the percentage of hemoglobin. I would go further and say that if the hemorrhage seems to be continuous, or recurs in large volume, I should transfuse regardless of either the hemoglobin or the blood-pressure. For, owing to the prompt action of the vaso-constrictors, the natural elasticity of the larger arteries, and the acceleration of the heart's rate which follows hemorrhage, the blood-pressure may be fairly well maintained for a time, though the total volume of blood in the arteries is considerably less than normal (Wiggers). Likewise the hemoglobin drops only as the blood is diluted with tissue fluid. In any case of profuse hemorrhage measures should at once be taken to provide for transfusion, and in spite of Ottenberg and Libman's warning against transfusion in acute first hemorrhages, I should say with Bernheim "When in doubt, transfuse.'

Other Liquids.—If there is no possibility of transfusion, salt solution, preferably of Ringer's or Locke's formula, may be introduced by rectum, by hypodermoclysis or intravenously. In its intravenous use it should be introduced slowly, and its quantity limited to 1,000 or 1,200 c.c. Physiologic salines do not interfere with the coagulation of blood (Crile), and may slightly stimulate the vasoconstrictor center (Pilcher and Sollmann) and where they are given to replace lost blood may maintain the blood volume for a sufficiently long period to save the life of the patient. But they have the disadvantage of increasing the volume but not the necessary blood elements, of decreasing the viscosity of the blood, and of changing its osmotic tension so that some of the fluid is before long lost to the tissues or excreted by the kidneys. But following hemorrhage this loss of fluid from the blood after saline is not nearly so rapid as when the blood volume has not been previously reduced (Crile). If the blood pressure is very low pituitary liquid or adrenaline solution, 15 minims (1 c.c.) may be added to the saline infusion fluid, the infusion being given very slowly.

Levin made a comparative study of the ability of saline solutions and transfused blood to replace blood lost by hemorrhage. In a number of dogs he let out enough blood to kill, allowing the heart to come to a standstill. When he replaced the lost blood at once with fresh blood by transfusion, the heart began to beat again, and in almost all cases the animal revived and in a very short time had returned practically to normal. When he replaced the blood with saline the heart began to beat again and kept it up for a time, but the animal did not revive. Of course, in such a case there was proportionately an enormous amount of saline introduced.

To *increase viscosity* and thus prolong the value of added liquid other than blood, less rapidly diffusible colloid liquids, such as a solution of acacia, 5 per cent. in Locke's saline, as recommended by Hurwitz, or a 1 to 2½ per cent. solution of gelatin in saline may be employed intravenously. Bogart, Underhill and Mendel found that after the introduction of colloidal gelatin solutions the blood retained the increased volume for an abnormal length of time. Gelatin is prone to contain putrefactive products and is less safe than acacia. Gelatin may also be used subcutaneously, and Lindberg has in this way introduced as much as 400 c.c. of a 10 per cent. solution daily.

To increase viscosity, Schreiber recommends 200 c.c. of 5 per cent. solution of glucose, though he has employed it up to 20 per cent. in strength. Kausch has used as much as 2,000 c.c. of 5 to 7 per cent. solution of glucose. Kuhn holds that glucose decreases coagulability.

8. *Other Mechanical Measures.*—In case of extreme exsanguination it is wise to bandage the limbs, to raise the foot of the bed high, to keep the body warm, and perhaps even to bind the abdomen tightly and put weights upon it after the method of Meltzer. For it is necessary to maintain the cerebral and coronary circulations at all costs or the patient will quickly die.

The use of an *ice bag* over the stomach is customary and may favor contraction of the stomach. But the theory that the application of cold to the abdomen results in constriction of the splanchnic arterioles is disproven by the work of Tice and Larson.

9. *Surgery.*—It is the consensus of opinion that while surgery may be called for in recurrent hemorrhages, immediate surgery is contraindicated in the presence of a profuse hemorrhage. It

has been estimated by Moynihan that not over 3 per cent. of profusely bleeding gastric or duodenal ulcers could be treated successfully by laparotomy. As a matter of fact, either spontaneously or because of or in spite of the medical measures employed, nearly all hemorrhages cease and as are not fatal. So that by the time we have decided that the hemorrhage is not going to cease, the patient is beyond the point of safety for an operation. Lindberg, of Faber's clinic in Copenhagen, tabulated 68 cases so severe as to raise the question of an emergency operation. It was decided in all the cases to give medical treatment. Only five of them died, and the autopsies showed that not one of the five could have been helped by surgery. These statistics together with statistics from other clinics, where operations were performed, have convinced Lindberg that surgical measures are never indicated in cases of acute hemorrhage from the stomach or adjacent bowel. Lund recently said, 'I have learned that it is poor practice, when the patient is depleted by hemorrhage, to open the stomach and try to grasp the artery in the bottom of an ulcer."

Summary.

The Aims in the Treatment of Profuse Hematemesis are three, viz.: 1. To stop the bleeding. 2. To overcome its effects. 3. To prevent its recurrence.

The *Treatment* is as follows:

1. Have patient very quiet, lying down, with head low, with a light ice-bag over the stomach, and with plenty of fresh air.

2. Avoid unnecessary manipulation.

3 Give a hypodermic of morphine sulphate, 0.015 gm. (gr. ¼) with strychnine sulphate 0.002 to 0.003 gm. (gr. 1/30 to 1/20).

4. Immediately after vomiting give by mouth a solution of thromboplastin, kephalin, coagulen or epinephrine.

5. In a case not of the portal congestion type, if the stomach remains distended, and the bleeding seems to persist, lavage with tepid water, and follow this by passing in a solution of epinephrine, thromboplastin, kephalin or coagulen through the tube. In portal congestion cases avoid lavage.

6. Prepare early for transfusion, and as soon as there are indications for it transfuse with careful watchfulness.

7. If there is severe exsanguination, bandage legs and arms,

raise the foot of the bed, bandage and put weights on the abdomen, keep up body warmth, and furnish fluid intravenously, subcutaneously and by rectum.

8. If transfusion cannot be done give intravenously Locke's or Ringer's solution containing 5 per cent. of acacia.

9. Finally, have a surgeon at hand to share the responsibility, but do not operate.

To prevent recurrence inject subcutaneously every 6 to 12 hours for one or two days, 10 to 50 c.c. of human, rabbit or horse serum, or a solution of coagulose or euglobulin; or a single dose of 100 to 500 c.c. of human serum; or inject intramuscularly a solution of coagulen, thromboplastin or kephalin.

If recurrence happens, resort to surgery after the bleeding has stopped, if necessary preceding the operation by transfusion.

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DISCUSSIONS.

Dr. Seymour Basch, New York City: I just want to point out that we should be prepared to do transfusion early, and be ready to resort to it when necessary. If we wait until the patients are almost exsanguinated, we wait too late. In the last case that I had transfused, the blood showed only 18% hemoglobin, and still the patient recovered. In those cases of severe gastro-intestinal hemorrhage of unknown origin that require operation, we must particularly bear in mind the great value of transfusion in rendering these patients better fitted to withstand the operative strain. From my own experience I am led to regard transfusion as the best method of treatment in severe gastro-intestinal hemorrhage.

Dr. Sidney K. Simon, New Orleans, La.: In regard to the matter of treatment of massive hemorrhages from the digestive tract in association with arterial disease, reported this morning, it struck me that the use of the stomach tube for lavage purposes was distinctly contraindicated, because of the obvious raising of the blood pressure that might ensue under the circumstances, I believe the best plan lies

in the use of large doses of morphine. In one of the cases, I employed nitrite inhalations, with apparently good results. This was in a case where there had been repeated hemorrhages throughout the day and night, and I was called in to take some decided step in the treatment. There is one point I should like to make regarding emetine: In the South, we use ipecac and its derivatives probably more than you are accustomed to use them here. We have found that only rarely does emetine produce vomiting. In some experiments that I was able to make a year or so ago, it was shown that the emetic property of ipecac is in fact due, in most part, to the alkaloid, ophalin, and not to emetin.

The employment of emetin in gastric hemorrhage, therefore, is not to be considered contraindicated on account of its emetic action. I quite agree with Dr. Bastedo, however, that as a hemostatic agent, generally, emetin is not to be relied upon.

DR. CHARLES D. STOCKTON, Buffalo, N. Y.: It is an admirable study of the physiological basis for the treatment of acute hemorrhage of the stomach. I feel that Dr. Bastedo has covered the ground very fully, and I think that in most respects the majority of men here will agree.

From personal experience, I find reason for the use of emetin. It certainly has the backing of wide foreign approval, especially among the French. I have used it repeatedly in intestinal hemorrhage, occasionally in gastric, apparently with marked success.

I should like to ask Dr. Bastedo on what ground he feels it proper to use normal saline. It seems to me contraindicated in all instances except when the patient is exsanguinated and life must be maintained through the slow injection of normal saline.

Coagulose was developed in Buffalo and was used extensively there because we desired to give as much opportunity as possible for clinical test. We have used it intravenously, subcutaneously, and intramuscularly, as well as by the mouth, and have rarely seen reason to question its efficacy. I have not seen reason to suppose it to be dangerous, except in one case of severe hematemesis in splenic anemia, ten days after splenectomy. Obstruction occurred, found on operation to depend on extensive thrombosis of the mesenteric artery; improvement in the patient was followed by a repetition of thrombosis in other arterial branches. Everything was thrombosed. It seemed impossible that such a large thrombosis could occur. In that case, we had used coagulose in large amount. I have since wondered whether we did not do harm by its use. However, we were dealing with splenic anemia, in which thrombosis is likely to occur anyway.

One point about the use of lavage is that this procedure seems to be safe and of value in early hematemesis. I should hesitate to use it in cases in which there are large coagula in the stomach. I have used it in cases in which hemorrhage occurred during lavage, and also when there had been hematemesis and only a small amount of blood thrown out. My object was to empty the stomach as quickly as possible, than using gelatin solution when available, and ending with a solution

of epinephrin. I am sure that adrenalin, used in this way, acts quickly and safely. Repeatedly I have seen the wash water change from bright red to pink, and then become colorless within a few minutes.

Dr. Thomas R. Brown, Baltimore, Md.: I enjoyed the paper of Dr. Bastedo extremely, but I want to ask him whether he does not feel that in the treatment of hemorrhage by these methods, we do not confuse *post hoc* with *propter hoc*, and think that the last drug is the best. I have tried a great many drugs, by mouth, and cannot honestly say that I have seen greater benefit from any of them, than from absolutely giving nothing but water with rest. There is no drug that is as efficient as morphia. I consider the administration of drugs subcutaneously or intravenously to be more effective than giving them by mouth, and I should like to ask Dr. Bastedo whether he can honestly say that any drug given by mouth has helped a sufficient number of patients to warrant him thinking it useful?

Dr. Julius Friedenwald, Baltimore, Md.: I am much interested in Dr. Bastedo's paper. I have never been able to assure myself that any local treatment is of much value in checking gastric hemorrhage; however, in our experience frequent small transfusions appear to have given us excellent results.

Dr. Jacob Kaufmann, New York City: As Dr. Bastedo has well pointed out, severe hemorrhage, when undisturbed, tends to bring about clotting, and we should take care not to interfere with this natural process by active treatment, and should give the patient complete rest. With regard to active measures, in case the bleeding does not stop, lavage has proved to me to be most efficient. We see, in gastric hemorrhage, conditions develop which much resemble the picture described as acute gastric dilatation after operations. I have seen enormous dilatations acutely develop with severe gastric hemorrhage. The dilatation goes along with accumulation, not only of food in the stomach, but of blood and secretions, which are often very acid. Gas forms, and causes great distention of the flabby stomach, often to a very marked degree. In one of my cases, when the tube entered the stomach the gastric contents escaped through the funnel with an explosive sound and were thrown against the ceiling of the room. If you evacuate these masses you give the stomach a chance to contract, which is one of the most efficient means of producing contraction of the blood vessels and clotting.

Another point of importance is that the greatly gas distended stomach interferes with the activity of the heart. One such case was considered hopeless by a number of physicians, because the pulse rate had gone to over 170. When I emptied the enormously dilated stomach and secured a lowering of the diaphragm, the heart immediately began to act differently, and the patient recovered from the apparently hopeless condition. In favor of lavage is furthermore the

fact that very often the bleeding continues on account of incomplete clotting. Lavage may remove an incomplete clot and allow the formation of a more complete clot.

One drug which may be useful was not mentioned, and that is bismuth subnitrate. To illustrate this I would quote a case published by Naunyn: The patient entered the hospital in very weak condition, the severe gastric hemorrhage being associated with violent diarrhoea. Gastric lavage stopped the bleeding, but patient died from exhaustion. At the post mortem von Recklinghausen took out of the crater of the ulcer 20 of the 25 grams of bismuth which had been put into the stomach after the lavage. The whole mass of the bismuth had accumulated in the crater of the ulcer and in forming a prop, had stopped the bleeding. That is a good illustration of the value of bismuth as a mechanical means.

DR. C. R. JONES, Pittsburgh, Pa.: I should like to express my appreciation of Dr. Bastedo's paper, and to mention one point in the application of some of the remedies he has mentioned. It has been my custom for some time to use adrenalin in ten drop doses, giving a tablespoonful dose of gelatin, of about the consistency of ordinary molasses or syrup. I believe that I get some effect from the constant application of the gelatinized adrenalin in contact with the ulcer, and, at the same time, I believe that we get some good results in lubrication. It seems to me that with a stomach that has been emptied or partially emptied of blood, especially if the ulcer be in the region of the pylorus, we possibly have some friction by contact of the opposite wall of the organ. At least, my recurrences had been fewer since I began to use this method of treatment.

DR. BASTEDO, closing: Most of the questions brought up have already been answered by the very enlightening discussion. There are, however, two or three things that I want to say.

In the first place, it is all "*Post hoc, ergo propter hoc.*" The percentage of patients who die in an acute hemorrhage from the stomach, from the lungs, or from various other parts of the body, is very small indeed. In Faber's clinic in Copenhagen, there were sixty-three cases of hematemesis in which the question of surgery came up. In all of these cases, they decided not to operate. Only five died, and these were found, at autopsy, to be cases that would not have lent themselves to surgery anyway. Therefore, if with the use of a coagulant the hemorrhage stops, that does not prove that the remedy causes it to stop. I might say the same of emetine. In any class of cases in which the hemorrhage tends to cease spontaneously I would take definite pharmacological evidence against a drug as of more value in my decision as to its use than clinical reports of the stoppage of hemorrhage in cases in which it has been used. Howell's work cannot be questioned in the matter of coagulation of the blood, and he has shown that emetin lengthens the coagulation time and diminishes the coalgulating power. Pellini and Wallace and others have shown that

it produces only a slight temporary constriction of the arteries, which is followed by dilatation, or it produces no constriction at all. Sollmann has demonstrated that it causes depression of the vaso-constrictor center and this results in vaso-dilatation. Therefore I believe that emetin should not be used. In this case of Dr. Kaufmann's, the thing that is the most interesting is that it shows how remedies come in contact with bleeding surfaces. After you examine a crater type of ulcer, you will wonder how any remedy could be given that would get at it. The center is deep down, and it is all buried under tissue, with overhanging edges. I wondered how any remedy introduced into the stomach could possibly reach there, anyway; but the presence of 20 out of 25 grams of bismuth in an ulcer crater shows that it did. So our remedies do perhaps spread over the wall of the viscus and stick where they can.

The other questions have been pretty well answered. There is just one thing more to which I wish to refer, and that is about this question of transfusion. I would reiterate: Get ready for transfusion early, and use it early, and would say, with Dr. Bernheim, "When in doubt, transfuse."

Calcium, I did not mention. It is utterly useless. There is no deficiency of it in this condition, and to affect the coagulation of the blood of a living human being it is required in enormous doses.

Dr. Max Einhorn, New York City, N. Y.: I should like to say a word in favor of emetin, and that my experiences with it have been favorable. I have applied it in gastric, and also in pulmonary hemorrhages, and I have seen, I think, good results. But I have never seen any vomiting occur from those doses which we gave, half a grain hypodermically, either once a day or every other day. I cannot guarantee it, but it made a good impression. Anyway, I did not see any bad results.

With regard to the other things that Dr. Bastedo mentioned, I think he was perfectly correct, and I fully agree with him that opium or morphine plays a great part in checking the hemorrhage and quieting the patient. I use it in most instances. Whether strichnine is so important, I do not know. I have seldom used it in my cases, and I had good results anyway.

There is one point that I should like to mention which has not been brought up. I have also seen good results in checking the hemorrhage and in trying to overcome the extreme degree of inanition, from the use of the duodenal tube. Fluid inanition is present in these cases, because of the hemorrhages. By giving the patient, soon after the hemorrhage, the tube, and letting it pass into the duodenum, we can supply the necessary fluid. As soon as we discover that the tube has entered the duodenum, we can place there whatever fluid we want, and I think that this has a tendency to hasten the recovery of the patient. I do not know that it checks the hemorrhage, but it is of great importance not to lose the patient, even if the hemorrhage is checked.

Dr. Arpad G. Gerster, New York City: I do not know whether Dr. Bastedo has considered one form of gastric hemorrhage which was very common in the early days of gastric surgery. I mean traumatic hemorrhage following operations. Considerable oozing into the stomach used to be looked on as almost normal. We expected a certain amount, and sometimes a considerable amount of blood to escape from smaller vessels cut by the surgeon's knife. The gastroplastic sutures were meant to be, but rarely were truly hemostatic. I remember the anxious hours following gastric operations in those early days. There was a strong prejudice against the use of the tube for emptying the stomach of blood. The symptoms so well described by Dr. Kaufmann were caused by the distention of the stomach by a collection of mucous, blood, all redolent of ether and gas. Finally if the patient vomited, and thus spontaneously ejected the contents of the stomach, and the oozing was generally stopped. This observation confirmed the old experience that a bleeding hollow organ, distended by partly coagulated blood, will not cease bleeding until that clot is evacuated. This is illustrated in the accoucheur's practice in relieving postpartum hemorrhages. Normally the contents of the uterus generally blood clot and liquid blood, are turned out of the uterus, whereupon the hemorrhage ceases. For identical reasons, as a routine in these cases, the tube is employed. We depend on it to such an extent that the house surgeon is permitted to employ evacuation without reference to the visiting surgeon. The effects are excellent in all cases, except where a large artery remains inclosed. In one case, a patient died of gastric hemorrhage following resection, in spite of repeated lavage. Post mortem examination showed that a considerable arterial branch had remained patulous through failure of the suture to close it. The mass suture of those old days was a very imperfect hemostatic. Since fine suturing of the cut surfaces was introduced (not treating the surface as a mass, but separately taking care of each bleeding vessel), these postoperative hemorrhages have become rare and have probably ceased altogether. However it may be it is necessary to relieve the patient from the torment of accumulated secretions, which, I believe, are copious on account of the use of ether. Even where there is no hemorrhage, but only nausea, lavage will bring great relief.

DEVELOPMENTAL EXERCISES FOR THE CHRONIC INTESTINAL INVALID.

By John Bryant, M. D.,

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Re-education of the higher centers through re-education of the lower centers is certainly not an original idea; but systematic development of muscle sense co-ordination and control, with a view not only to developing muscle control, but to correcting certain mental tendencies of the chronic intestinal invalid, is either a new application of an old principle, or one which on the basis of the results obtainable is not sufficiently known and used.

The thin type of chronic intestinal invalid, habitually suffers from numerous disadvantages somewhat outside the immediate province of gastro-enterology; but often his, or even more often her margin of reserve is so slight that success in treatment results only from patient and diligent attention to all possible points of attack. The present paper is concerned only with a simple and efficient method of influencing the actions and inter-actions, of the nervous-mental and muscular systems of the chronic intestinal invalid. The method results from a study of the following circumstances:—

1. The total of muscular energy available per hour is in these patients below normal. Yet reckless, not to say useless, rather than conservative expenditure of this limited energy, is the rule.

2. The fatigue limit of the existing musculature is usually below the normal, owing to toxic or other depressant influences.

3. Afferent sensory stimuli may not exceed the normal in number, but;

4. The central inhibitory mechanism seems to function less than normal.

5. The total number of efferent motor stimuli is therefore in excess of normal, because;

(*a*) The normal ratio between afferent sensory stimuli and effective motor discharges is disturbed.

(*b*) Minimal sensory stimuli may produce maximal motor

discharges, owing to the absence or diminution of normal inhibitory processes.

6. Continual excessive motor discharge causes constant wasteful hypertonicity of the muscles.

7. Hypertonicity, and a frequent inability to completely relax muscles not actively in use, hasten the onset of fatigue in already poorly developed muscles, and result in a loss to the organism of perhaps 50 per cent. of its total available supply of energy. This lost energy is consumed in the wholly unprofitable business of overcoming unnecessary friction, due to inability to relax, for example, a flexor when its normal opponent muscle is in use.

8. The fatigue posture is in itself a serious contributing factor in the early production of general muscular exhaustion.

No sane man could see an engine racing itself to pieces without a desire to throttle it down to a rational speed. Why should the physician sit idly by and watch a high strung human mechanism running wild with its rheostat acting either poorly or not at all? Such a spendthrift mechanism is surely destined to squander its little store of energy and end in physical bankruptcy. In a word, scarcely deserving of the title human, such a mechanism may become reduced in efficiency almost to the level of the spinal laboratory animal in whom every sensory impulse yields its immediate even if useless motor response.

The future of the patient who suffers from such pathologic sensori-motor imbalance is fortunately not necessarily always dark. Once recognized, regardless of whether the etiology of the condition be traced to heredity or to faulty early education or to some disturbance in adult metabolism, the problem presented is the same. Its solution lies in the direction of

(*a*) Increased inhibition of afferent sensory stimuli.

(*b*) Decreased discharge of motor impulses which produce only a purposeless or inefficient expenditure of muscular energy.

Working at first to improve the deficient musculature of the chronic intestinal invalid, it soon became evident that the following formula is to a considerable extent reversible:—

MENTAL
CONTROL *CONTROL*
MUSCLE

To increase or to decrease one of these factors is automatically to increase or to decrease the other factor. Therefore, since *muscle* is more tangible than *mind,* it is obviously easier to begin with the re-education of the former. Re-education of muscle sense may, in short, be said to constitute a kindergarten or preparatory course to re-education of the *mind,* on completion of which one may, if so disposed, proceed to the employment of some of the more abstruse methods for developing actual brain control.

It is little short of astonishing to discover how very slight is the acquaintance of the average human with the muscular workings of his own body. The patient is scarcely less astonished when informed for the first time, that he should be able to move at will his abdominal or other muscles, in precisely the same way that he can move his individual fingers without moving his entire hand. But when once the idea that his body should be his servant, has penetrated the mind of the patient, the physician will soon himself be surprised. He will in fact be astonished to find how assiduously and with what determination the patient whom he had thought lackadaisical or indifferent, will work to get a real control of his or her muscles.

In early attempts, although the object sought was very definite, the process of transferring the idea to the mind of the patient in a form which would result in the desired action, often proved difficult.

Experience has proved that there are four essentials to success in the re-education of muscle sense or muscle control:—

A. The central nervous circuit to the given muscle being rusty, extraneous assistance must be offered; this is done by two devices:

1. Some general muscular movement is performed which if executed of necessity produces contraction of the desired muscle group or single muscle.

2. Through the sense of sight or touch or both, the patient is made to experience the actuality of the contraction of the given muscle during its response to a central motor impulse. It is gratifying to see how rapidly muscle sense perception sharpens enough to enable the patients to dispense with these external aids.

B. The rate of muscle contraction or muscle movement is

exceedingly important. This should never exceed a rate of five seconds per foot of linear distance, and at first is better slowed toward ten seconds per foot. Conducted at this rate, a supposedly normal individual not infrequently shows slight degrees of unsuspected muscular inco-ordination. This tends to disappear with practice, and this visible demonstration of actual improvement is in itself no small factor in the eventual recovery of the patient.

C. The force of contraction of the given muscle must be always at or near the maximum of which the patient is at the moment capable. This capability may constantly differ but always tends to increase.

D. A given muscle must never be driven beyond the point of the first appreciable onset of fatigue. It is, however, desirable to reach this point. For example: at first, one slow firm contraction may be sufficient where later ten may not suffice. Furthermore, between two successive contractions there must always be an appreciable interval of complete relaxation (checked again at first by a hand placed upon the muscle whereby to control its tension).

Progress, when the above points are insisted upon, is usually gratifying and continuous; but the total time required for satisfactory muscular re-education must often be counted in months. Cases with actual organic nerve or muscle lesions are, of course, not included in this prognosis.

What, it may be asked, has all this to do with mental re-education or control? It has very much to do with it. No one can even perform these slow exercises once, properly, without keeping his or her mind very definitely and continually on the job, during the active performance of the exercises. Continued mental application to any subject spells mental concentration. Mental concentration, with its implied ability to deconcentrate or avoid undue irritation from undesirable afferent stimuli, is certainly one prerequisite to mental control. Evidence of this gain in mental control is frequently volunteered by patients, pleased at finding themselves able to pass unruffled through experiences which would formerly have left them completely "unstrung."

A second prerequisite is the ability to evaluate the necessity for, and the intensity of, efferent motor impulses, with a view to obtaining a maximum result for every expenditure of nerve

force or muscular energy. Usually in our invalid this form of discrimination is lacking. He tends ever to move at top speed as long as he is able to move at all, regardless of the scale of urgency of the given action; here is a lack of efficiency which in the industrial world would be remedied by adjusting the governor of the engine. In the industrial as well as the human mechanism the greater the speed the more disproportionate becomes the liability to wear and tear. Hence the necessity of teaching the invalid to travel at his optimum speed, reserving his expensive maximum bursts for maximum necessities.

A third and perhaps the most vital element in mental control, is will power. This factor is automatically developed by the prescribed exercises, for the simple reason that at least some effort of the will is always implied by their accomplishment; also, certain exercises are done against increasing resistance which can only be overcome by the active and positive use of the will to succeed in them.

Lastly, in the worst cases, with twenty- or thirty-year histories of successive medical or surgical failures, cases in which hope is moribund, nothing may be accomplished before conviction is brought to the patient's psychic self. In such a patient, the vision of failure must be obliterated, hope galvanized into permanency, and the torch of faith in a better future must be made to burn with a fierce intensity. Create this atmosphere, enforce the prescribed exercises so that soon a patient may see for himself his actually demonstrable progress, and the mental problem of the chronic intestinal invalid will presently be found to have almost if not quite vanished. Success in creating the desired atmosphere, depends, of course, upon the so-called personal equation; it depends no less, however, upon knowing in detail what one is trying to do, knowing how to transmit this detail in effective form to the brain of the patient, and in knowing that one has previously been successful in accomplishing the desired results.

Three groups of simple exercises have been developed, upon the basis of increasing experience. These groups—

(*a*) Remould the torso.

(*b*) Reorganize the general musculature.

(*c*) Restore co-ordination and balance.

Of these three groups, the third (*c*) is added last and varied according to the indications revealed by previous work.

The second group (*b*) consists of one simple exercise for each of the larger muscle groups. For example: anterior group, lower leg, brought into action by raising the balls of the feet off the ground so that the weight when standing comes only upon the heels. To bring the posterior group of the leg into action, it is only necessary to rise slowly upon the toes when standing erect. Similar exercises for other muscle groups will readily suggest themselves; increasing weights, from one pound up are often useful in carrying out this group of exercises.

The first group (*a*) comprising a few exercises yielding results fundamental to the general health of the patient, will be given in detail. A prolonged etiologic study of the congenital visceroptotic invalid has illuminated the following muscular circle: the loose viscera depend chiefly for support upon the activity of the lateral abdominal muscles; these muscles are most efficient only when working from lower ribs held firmly at or near full expansion, a condition which also enlarges the upper abdominal cavity; elevation of the lower ribs implies contraction of the intercostal muscles and is greatly facilitated by erect posture with slight arching of the back; erect posture depends upon proper activity of the erector spinæ group of muscles. It will be seen that the muscular trail leads to the erector spinæ group, and since all the muscles mentioned are usually in a deplorably weakened condition, passive orthopedics have been in so far as possible discarded in favor of very carefully graduated active exercises. As previously stated, the approach of fatigue is invariably a contra-indication to further effort on the part of the patient by the muscle group involved; likewise, the rate of movement, thought near maximum in intensity, must be limited to between five and ten seconds per foot and muscular control must be absolute until a given motion is completed. With these considerations in mind, the following exercises are performed:—

1. Erector spinæ group.

Position: patient lies face down, legs extended, with arms straight beside body or with hands upon buttocks so that arms may not assist back muscles.

Method: with head straight, resting upon chin, patient is told to riase head and back slowly and see how much of the ceiling he can see, after which patient sinks slowly to original position;

head and back must not rotate sideways. Between each attempt there must be complete muscular relaxation, with one or two slow full inspirations and expirations.

2. Respiration group.

Position: patient resting flat upon back to avoid collapse from the unaccustomed hyperpnea, and to avoid lifting the extra weight of the arm and shoulder girdle during respiration.

(*a*) Intercostals above nipple line.

Since in most of the patients under discussion, respiration is already being carried on almost wholly above the nipple line, to the exclusion of normal use of the lower muscle groups, (*b*) and (*c*), further consideration of this group (*a*) is dismissed.

(*b*) Intercostals below nipple line.

It is essential that the costal angle be widened from the acute angle usually found in these cases, to something approaching the normal, which is a full right angle; by this means at least 3 inches should be added to the circumference of a narrow lower thorax, with corresponding relief for the compressed upper abdominal cavity. Incidentally, the raising of the diaphragm tends to dissipate certain circulatory phenomena concomitant with the existence of the "drop-heart" so commonly present in the narrowed thorax.

Position: patient reclining flat upon back with legs extended. Method: instructor places his hands over the lower free ribs on either side, and tells the patient to push his hands out by the force of his respiration. This soon localizes the respiration, and soon one may demonstrate to the patient that these same ribs may be "sprung" outward by muscular effort alone without any inspiration, and that by the same muscular effort these same lower ribs may be kept constantly in this expanded position of full inspiration. The next question from the patient invariably is, "where shall I breathe then?" The answer is, "in the epigastrium, with your diaphragm."

(*c*) Diaphragm.

The diaphragm is a powerful muscle which was especially designed for the purpose of respiration, although at the present day it seems unusual to have it used for the purpose; consequently it may often be difficult to localize respiration to it. The fullest type of diaphragmatic breathing necessitates, of course, during expiration, the additional complementary action of the lateral abdominal muscles, a result greatly to be encouraged.

Method: with lower thorax (*b*) in full expansion, instructor places his hand upon the epigastrium and makes the patient take a series of very short rapid breaths with mouth wide open. The intercostals have no time to act; immediately, the respiration may be made less rapid and deeper, and the patient soon has learned that he can get all the breath he can use in this manner, with distinctly less effort than was required by him by his previous and faulty method.

3. Abdominal group.

Position: patient reclining, as in previous exercise, to eliminate the extra effort necessitated if in a standing position by working against the downward thrust of gravity.

(*a*) Diaphragm.

To learn that the diaphragm is an important abdominal muscle, one has only to listen to the way in which its free action shakes up wind and water in a sluggish intestine. This commotion is very gratifying to the patient, since it is an audible demonstration that he is actually doing something to his "insides."

Method: as in previous exercise, 2 (*c*).

(*b*) Lateral abdominal muscles.

Even in the presence of a powerful rectus, these lateral groups are often exceedingly poorly developed, though their possessor may be something of an athlete. This general neglect is the more incomprehensible, since it is primarily upon these muscles that the position of the viscera depends, especially in the congenital type of invalid in whom the visceral attachments are always most lax. To prove this, it is only necessary to fluoroscope such a patient after the ingestion of bismuth. It will at once be obvious that the position of the stomach and often of the entire transverse colon depends within a perpendicular range of some inches, wholly upon the degree of laxity of tension of these lateral muscles.

Method: patient reclines flat upon his back without lateral deviation; with the right hand resting transversely upon the abdomen over the lateral abdominal muscles so that its middle finger-tip is just within the left iliac spine, patient with head raised a few inches moves his body laterally so as to approximate the left hand toward the left ankle and then returns slowly to the resting position. During this maneuver the patient feels beneath his hand the desired muscular contraction. Eventually, neither the sensation under the hand nor the bodily movement is

required; the action of the will is sufficient, and through his sharpened muscle sense the patient is aware that the desired muscular contraction is being executed under perfect control. Between each full movement, relaxation and respiration are required. For the right abdominal muscles, the proceeding is reversed.

(*c*) Rectus abdominis muscle.

Position: patient flat upon the back without lateral deviation.

Method: with hand upon the epigastrium, patient slowly raises head and shoulder several inches toward the sitting position until firm contraction of the muscle is palpable, and then sinks as slowly back to his reclining position.

To these few fundamental exercises, many others are added according to circumstances, but the underlying principles do not vary. Simplicity, and slow, firm, controlled action are imperative, whether or no resistance and balance are also involved. Results justify the labor implied, for one may assure a patient that at least a considerable degree of improvement will attend his faithful efforts. Ultimately, it is possible for the patient to maintain the expanded thorax and contracted lower abdomen indefinitely, in a standing position, and for the most part only at an expense of subconscious mental effort.

Summary.

The chronic intestinal invalid is inefficient as a mechanism. Mental and muscle control are deficient. In him inhibition of afferent sensory stimuli is less than normal; motor responses being excessive, the result is premature fatigue. Available energy must be conserved. A method of exercise is described which not only develops the musculature but teaches the invalid to conserve his energy. Inhibition is increased, and motor discharges are controlled.

The results are beneficial since the patient learns to control his muscles and through them his mind. The method may be applied in patients where simple development of the torso or of the general musculature is desired, equally with those in whom an actual increase in muscle and mental control is essential to any approximate return to health. Most important of all, the graduated patient will have learned a method by which he can keep himself in health, without the use of extraneous apparatus.

338 Marlborough Street.

GETTING RESULTS WITH THE CHRONIC INTESTINAL INVALID: ONE YEAR WITH AN OUT-PATIENT CLINIC.

By John Bryant, M. D.,

BOSTON.

In July, 1916, there was opened at the Peter Bent Brigham Hospital, what is believed to have been the first clinic devoted exclusively to an attempt to relieve the chronic intestinal invalid of some of the factors which are operative in causing his chronic attendance at hospitals. Routine treatment obviously fails frequently. Physical examination often reveals nothing more than poor development and general debility, or the case may be classed as pre-tubercular. From the laboratory may come a negative Wassermann reaction and a report of some degree of visceroptosis. Nothing in particular being found, nothing in particular is done, save to give vague directions concerning hygiene. These patients abound in all hospital out-patient clinics, and it is not common sense to presume that all these wage earners prefer sitting around hospital corridors to doing their regular work. The present note is one answer to the old question, can anything ever be done about it? In a small, and at first experimental, way, something has been done about it.

The general method of approaching the problem was based upon more than five years of intensive study. The details of treatment had to be evolved. In view of the generally negative laboratory reports on these cases, it was concluded to conduct the work in so far as possible without the aid of scientific apparatus. The equipment therefore consisted of an examining table, two chairs and a desk; this appeared to be the irreducible minimum. If this point of view appears reactionary, it may be replied that some of my patients had been through periods of prolonged sicentific observation in the wards of one or more large modern hospitals without improvement, yet these same patients, after varying lengths of time at the clinic, professed to be very much improved. Laboratory tests do not cure these people, and on the whole, specialized group medicine has little to offer them. The

reason is not far to seek. The proper medical perspective is lost as the patient is shunted from one specialist to another. Here especially is needed the modern edition of the general practitioner, one who to a broad grasp of medical problems adds a really keen interest in the thousand and one petty details of the home trials and tribulations of his patient, and one to whom time is no object as compared with the possibility of rearranging and more effectively ordering the routine of these same petty details,—details perhaps petty in themselves but often containing in their study the long sought possibility of better health.

The clinic has been conducted on a bi-weekly basis. Progress is at best so gradual that there is little profit in greater frequency. The work has been wholly personal except for rare special laboratory work when this has been considered indispensable, and excepting valuable social service work by Miss Cheney; consequently the total number of patients seen has been less than 100, with an attendance averaging eight to ten a morning. The time factor has been completely disregarded, but has averaged about three hours; one day with everything going well fifteen patients might be disposed of in two hours, and the next day four hours might be consumed in trying to benefit five or six patients.

The first patients were received from the medical out-patient service of the Brigham hospital, without further qualifications than unsatisfactory progress and continued complaint of digestive disorder. Later, cases were referred directly from the wards, and still later from other hospitals and local physicians, a few coming more than a hundred miles to attend the clinic.

Often the intestinal picture was found complicated by definite though previously overlooked organic disease, such as tuberculosis asthma or gall-stones, or by multiple abdominal surgery, concerning which it may be remarked that the ease of cure or near cure of these patients often seems to vary somewhat in inverse proportion to the amount of abdominal surgery to which they have been exposed. Except in acute or malignant cases, surgery is not indicated until after months of medical care.

The results of treatment at the clinic, the duration of which in individual cases varied from days or weeks to months, are

somewhat as follows for the 76 cases seen often enough to make their names worth recording:—

	Per cent.
Disappeared	22
Failures	4= 7
Improved	14=27
Improved plus	36=66
Total	76

In considering these figures it is perhaps fair to discount the group of 22 cases marked "Disappeared." Since the entire group of 76 cases represents previous failures on the part of the medical profession, it would be remarkable if some cases did not remain unconvinced or unimproved. It is definitely known, however, that some others of this group considered themselves completely cured of their previous ailments even after very short acquaintance with the clinic. Thus one man was seen only twice, yet in the course of the following two months he was responsible for sending five or six of his friends to the clinic in the hope that they might receive equal benefit.

Flat failure was the result in 4 cases. Three were women: one had lived through five abdominal operations and was said to be facing another; a second woman had probably gall-stones; the third had some form of pelvic disease. The man, aged twenty-six, was an interesting case. He was in apparent good health until subjected to exposure in the form of a train caught in a blizzard. The steam heat was cut off for hours. He caught a severe cold, was taken to a hospital, and shown to have marked acute nephritis. In chronic form this still persists. Previously regular, since his exposure to cold, he has suffered from violent constipation which has not yielded to any measures yet attempted.

In the 14 cases considered as "Improved," are 3 men and 11 women. Although slight to some improvement over the original condition is certain, their progress is not considered satisfactory.

Concerning the status of the 36 cases considered as "Improved plus," there is little doubt, although it contains, for instance, 2 female asthmatics, one of whom probably also has tuberculosis. No claim to cure is made for any of this group. It is, however, something that all are distinctly better able to carry on their daily life. Of these cases 6 were men and 30 were women.

Comment.

Although the total number of cases is not large, there is shown, considered the depressing character of the material, a high percentage of improvement. With selection of the type of case, it is reasonable to expect even better results. In my own private cases, for instance, of a group of 26 chronic intestinal invalids, with records of five to twenty years of consistent medical failure at the hands of recognizedly skillful men, all, or 100 per cent., are very much improved. As the work at the clinic has progressed, certain etiological factors have been demanding more and more consideration. First and by long odds foremost is the question of *Fatigue.*

Fatigue is the reaction of every individual strain which for the given individual is excessive. It is immaterial whether the strain be excessive or whether the individual be asthenic or otherwise defective; the result is the same, on a scale varying from acute or chronic fatigue to exhaustion, collapse and death. Examples of the approximately normal individual unable to withstand excessive strain if this be sufficiently great or sufficiently prolonged, are altogether too plentiful at or back of the trenches in Europe today. Examples of the subnormal individual unable to withstand approximately normal strains, are even more numerous in our own hospitals and homes. Faulty heredity, faulty feeding, and faulty education of hte child are certainly to blame, and indicate that real preventative medicine for these invalids begins in childhood.

As in chemistry one speaks of unstable ring compounds, so perhaps we may refer to an unstable health ring composed of at least four elements, as follows:—

INDIVIDUAL
RESISTANCE ENVIRONMENT
FATIGUE

To standardize or to stabilize any one of these elements, is by so much to increase the chance for health of the given individual. It will be seen that three of the four factors given are external, and it will at once be obvious why treatment which is limited to only one of these factors, usually the individual, is less likely to be successful than treatment which is directed

to the simultaneous adjustment of all four factors. The latter method demands more of the physician, and requires a knowledge of other things than pills and powders, but the additional labor entailed is more than compensated for by the more satisfactory results obtainable, and by the lasting gratitude of the patient.

Treatment.

The period of treatment may be divided into three phases, as follows:—

A. Acute.—External and internal rest is judiciously applied, in repeated small doses, in such manner as not to impair the patient's remaining will power,—his will to get well, his best asset.

B. Subacute.—External exercise is cautiously begun, great care being exercised to avoid the production of fatigue. During this phase the internal rest is continued by means of bland food and the other means which will suggest themselves for reducing to a minimum all strains upon the metabolism of the patient.

C. Chronic.—External and internal exercise is applied in slowly increasing doses.

During these phases of recovery, extending perhaps over six months to a year, in addition to taking all possible measures for reducing the strains from which the patient cannot escape, of making the environment as favorable as possible, and of increasing to the maximum the patient's resistance, three factors, more strictly speaking medical, have been found valuable. These are—

1. Diet.
2. Exercise.
3. Ductless gland preparations.

The diet, at first as bland and as unirritating as possible, may very gradually be approximated toward the normal. It has been found helpful, however, at first to omit eggs, meat and fish, and then to restore these valuable foods to the dietary by means of alternating restricted and full diet days. Thus at first Sunday might be a full diet day followed by several days of restricted diet. Eventually a complete full diet is possible, but probably the patient may never look forward to more than every other day of full diet without also looking forward to some return of symptoms.

A system of very slow exercise* has been evolved which has proved exceedingly valuable in clearing away mental cobwebs no less than in restoring to the patient some adequate control of his motor mechanism, whereby to conserve to the utmost his ever too little store of available energy.

In spite of the fog of quackery which at times almost obscures the gland preparations from view, and acknowledging the difficulty of proof of cause and effect, it is my conviction, based upon prolonged observation, that not infrequently the judicious use of these preparations enables the patient to progress an additional step towards more complete recovery.

Conclusion.

Proof has been presented that the future of the chronic intestinal invalid may be less black than it has been painted. The results given in this brief report indicate that he who will take the trouble and time, may without elaborate apparatus salvage a high percentage, when and where he pleases, of a class of patients too commonly and too complacently assumed to be merely neurasthenic or otherwise uninterestingly hopeless. Inability to reproduce the results given reflects more upon the attitude of the medical profession than upon the medically unknowing and thus far too little educated patient. These patients have cried aloud into a deaf ear of medicine and have turned by the score and hundreds to the various cults, to an extent which is a reproach to the modern physician.

338 Marlborough Street.

DISCUSSIONS.

Captain Bryant, closing: I thank the gentlemen very much. If I may have another couple of minutes, I would say that this paper was written in reference to one class of patients. There are two classes: one, rich; and the other poor. With the rich, you have no excuse for failure, for their time and money are absolutely their own. With the poor people I started with the conditions for success as bad as they could be from all directions. That is, I was without scientific assistance, and had the worst class of patients that I could get, so as to see what could be done with poor people. Many of these were women with four to six children. They could not afford nurses; they

*See Dr. Bryant's paper, "Developmental Exercises for the Chronic Intestinal Invalid," p. 625.

had to do their work and look after their children. In spite of that, they got well or had temporary improvement. As was said yesterday about the patient who vomited blood in the trial, I think that some of my patients will probably be down flat again as soon as they get too far from the way in which they were taught to live. If we take enough time with individual patients to teach them how to live in the best way under the conditions that they cannot avoid, and then aim to improve the conditions as much as possible, we can do a great deal even in these poor people. This problem boils down to enormous wasteage of energy. They do not have much energy to start with, and if they waste it, they do not have enough left to carry on their daily life.

Muscular control is valuable in freeing these invalids of phobias. One patient had been doctoring for twenty years, it took just one year to get her on her feet. She gave a list of ninety doctors, fifty of whom were in Boston, that she had consulted within the last ten years. They had included specialists of all kinds. She was scared of everything. As she got some muscular balance by means of the balance exercises, there was a visible improvement in her mental processes. I require my patients balance on one foot with slow exercises. You will find that this may at first be impossible. The patients fall all over themselves. One reason for their fears is that they have not a proper understanding of their motor apparatus. I did not do anything to this particular patient but show her how her legs worked, and that she could stand on one, instead of two. She can now walk anywhere without phobias. Most patients do not know how their own legs work.

I will read one paragraph from the conclusion in the first paper.

"Results indicate that he who will take the trouble may, without elaborate apparatus, do a great deal for patients too complacently assumed to be neurasthenic or hopeless. These patients have, however, gotten tired of medicine, and have turned by the hundreds to the various cults in a way which is a reproach to modern medicine.

ON THE EXAMINATION OF GASTRO-INTESTINAL PATIENTS IN BASE HOSPITALS.

By Seale Harris, Major M. R. C.,

Section on Gastro-Enterology in the Division of Internal Medicine.

The following was prepared for the information of gastro-enterologists assigned to duty in base hospitals.

General Considerations.—When the Surgeon General planned the work of the new army hospitals his first consideration was that our sick and wounded soldiers should have the benefit of the best medical talent and the most complete equipment in every branch of medicine and surgery. His wishes have been carried out in a remarkable way, because never before in the history of warfare have there been hospitals so thoroughly equipped, with such an array of medical and surgical talent on their staffs, as are found in the United States army camps.

When we consider the fact that the digestive diseases occurring among more than a million men are being treated and studied by physicians who have had special training in that specialty in medicine, and who are devoting all their time to hospital work, we realize the wonderful opportunities for collecting clinical data that are presented to gastro-enterologists who are assigned to the base and general hospitals in the army.

From the scientific viewpoint, and to make the medical history of the war of greater value, at least in so far as diseases of the digestive organs are concerned, it is desirable to standardize as far as possible in all the hospitals. It is not intended, however, to interfere in the least with the methods of diagnosis or treatment that each gastro-enterologist has been employing to his satisfaction nor to prevent his pursuing any line of original or research work in which he is interested. It is with the idea of helping to standardize methods that the following suggestions are offered for the information of gastro-enterologists assigned to base and general hospitals. It is intended merely to outline methods for examining patients in military service and to discuss briefly some of the problems in diseases of the digestive organs with which the gastro-enterologists in army service may have to deal.

The Anamnesis in Digestive Diseases.

In civil practice, the anamnesis is of great importance in the diagnosis of digestive diseases; but, in the examination of the patriotic soldier, who may try to conceal his physical disability in order to get foreign service, or, of the malingering conscript, who may feign all sorts of symptoms in order to be discharged from service, it is sometimes necessary to disregard statements of the patient, as to his past history and present condition. In any event, the gastro-enterologist must estimate the value of the patient's statement, and often the diagnosis must be made from the physical examination, laboratory findings, and X-ray examinations. With modern methods of diagnosis, positive conclusions can be reached in a great majority of cases, without the aid of the patient's medical history, though the difficulties of accurately diagnosing abdominal conditions should never be forgotten.

It is essential in all cases of digestive disease, that thorough and complete examinations be made, and that full histories be taken. It is also important that the histories be uniformly and systematically recorded by all gastro-enterologists. The regular forms or blanks for the records of the hospital should be carefully filled out, but, additional history blanks for digestive cases will be supplied to each of the hospitals to which gastro-enterologists have been assigned. In making the records of patients in army hospitals, gastro-enterologists should remember that they are writing a part of the medical history of the war; and to make it of greatest value, a report of every case must be accurate and complete.

The serial case history is the simplest and most satisfactory mentioning the symptoms described by the patient and the abnormal conditions found on physical and laboratory examinations, and omitting references to negative findings except where they may have some bearing on the case. It is important, however, to have a systematic order in recording symptoms and results of physical and laboratory examinations. The following scheme for history taking in diseases of the digestive organs is suggested for the reason that it is desirable to have the records in all hospitals conform to the same plan.

Scheme for History Taking.

Recording the Complaint.—It is ordinarily best to begin the history with a statement quoting the patient's own words in de-

scribing his symptoms. The gastro-enterologist should get fixed in his mind the complaint from which the patient desires relief.

Family History.—Record age and state of health of parents, brothers and sisters. If any are dead, give ages and causes of death. Is there a family history of tuberculosis, carcinoma, nervous or mental disease, alcoholism, nephritis, or paralysis? If overweight or underweight, is it a family characteristic?

Previous History.—A serial history of previous illnesses in chronological order, beginning with the diseases of childhood, should be recorded. Inquiry should be made regarding previous infections, particularly focal infections (periapical abscesses, tonsillitis, injuries, etc.), typhoid fever, rheumatism, pneumonia, tuberculosis, etc. The relation of digestive diseases to other organs should always be kept in mind, and the history of disease of every organ in the body should be recorded. It is best to question the patient regarding the previous symptoms of the different parts of the body, beginning at the head and going downward to the extremities; first, disease of the eye, ear, nose and throat; then the teeth, as to abscesses, pyorrhea, etc., condition of teeth, whether the patient wears plates, bridges or crowns; then the repsiratory and cardio-vascular systems genito-urinary diseases; skin; nervous symptoms, such as fatigue, worry, insomnia, etc., finally the extremities.

Previous Digestive History.—Particular inquiry should be made regarding the history of previous diseases of the digestive organs such as bilious attacks, acute indigestion, jaundice, constipation, diarrhea, hemorrhoids.

Habits.—The habits of an individual play an important part in the etiology of digestive diseases. Over-eating, particularly of meats and sweets, insufficient nourishment or unbalanced diet, excessive use of alcohol, tea, coffee, coca-cola or other caffeine beverages, may be the cause of many symptoms which make the individual feel that he has a serious digestive disease, but which will disappear when the habit is corrected.

Present Illness.—A serial history of the present illness should be carefully recorded. It is important to note the date and the character of the initial symptoms, as well as to describe the subsequent symptoms, as they appear. If there is a history of repeated attacks, the digestive disturbances with the dates and symptoms of each should be recorded.

Pain.—Differentiate carefully between pain and fullness or discomfort. If there is pain, give the location, its character, whether aching, burning, gnawing, colicky or boring. Is it a steady pain or does it intermit? Does it appear before, after, or during meals, or has it no relation to the time of taking food? Is it influenced by coarse food, or warm or cold drinks? Is it relieved by eating, or by drugs, soda, etc. If there is fullness or discomfort, is it related to meals or character of food?

If there has been vomiting, state time of vomiting and character of vomitus. Does vomiting give relief of symptoms? Has he ever vomited blood. Note the appetite, whether there is anorexia, bulimia, or thirst. Condition of bowels, is there constipation or diarrhea? Do the stools contain mucus, pus, blood, etc.? Inquire of the amount of urine and frequency of micturition.

If there are symptoms involving other organs, they should be recorded, because very often digestive diseases depend upon and are associated with pathological conditions of other organs.

Weight.—The patient should be weighed on the date of his examination, and he should be questioned as to his previous gain or loss in weight. He should be weighed once a week while in the hospital.

Physical Examination.

The record of the physical examination is as important as the history of the symptoms. The examination should be thorough and systematic, giving attention to every organ or part of the body from the patient's head to his heels. The abnormal findings should be recorded in the following order: (1) head, including teeth and tonsils; (2) neck (thyroid); (3) lungs; (4) heart; (5) abdomen; (6) extremities. The temperature and blood pressure should be taken and recorded in every case.

The rectum should be examined digitally and with proctoscope in all cases of constipation, diarrhea, painful defecation, or where there are other symptoms suggestive of an anal or rectal lesion, unless the cause of the trouble is apparent.

A brief discussion of the physical examination of the abdomen may be worth while, since it is of great importance in making the diagnosis in digestive diseases.

Inspection.—Inspection of the abdomen may reveal tumors,

and in emaciated individuals the outlines of the stomach may be visible, also peristalsis of the stomach and intestines in cases of pyloric stenosis or intestinal tumors.

The general contour of the abdomen should be noted, and if there is habitus enteropticus the measurements from the ensiform cartilage to the umbilicus, and from this vertical line to the anterior axillary fold, should be recorded

Palpation.—Superficial palpation may give important information regarding the location of tender areas, or muscular rigidity over the stomach, intestines, gall-bladder and appendix. Deep palpation may locate and determine the size of abdominal tumors. The effort should be made to palpate the spleen and kidneys in every case.

Fecal masses may simulate abdominal tumors, making it necessary in some cases to clear out the intestinal tract with a laxative before the second examination. An expansile or pulsating aorta has been known to be mistaken for an aneurysm or abdominal tumor.

Percussion and Asculation.—Percussion and asculation give but little information in the diagnosis of gastro-intestinal diseases, though in some cases the stomach may be outlined by auscultatory percussion. The X-ray, however, is the only accurate method for outlining the position and size of the stomach and intestines.

The Laboratory in Gastro-Intestinal Examinations.

Test Meals.—If time can be allowed and the patient does not object too strenuously, it should be a routine to give each person referred to the gastro-enterologist, an Ewald, or Dock, test breakfast, removing the contents in an hour by the expression or aspiration method. The fractional method of examination of the stomach contents, as employed by Rehfuss and others, may give information of value to supplement the usual method.

Value of Chemical Examination of Stomach Contents.—Contrary to the opinion of many surgeons, and some internists, the chemical examination of the stomach contents is of much value in making the diagnosis of ulcer and carcinoma of the stomach, as it is in many other gastric diseases. Hyperchlorhydria does not always mean ulcer, nor does achlorhydria necessarily indicate carcinoma; but in ulcer, except in the long-standing case, there is usually an increase in hydrochloric acid; and in the great

majority of cases of carcinoma of the stomach there is absence of hydrochloric acid, and the presence of lactic and other organic acids in the stomach contents. Therefore, when there are subjective symptoms of ulcer, with a hyperchlorhydria, and the presence of occult blood in the stools, the diagnosis of ulcer is probable; and when there are other evidences of gastric carcinoma, the absence of hydrochloric acid, and the presence of lactic acid in the stomah contents is certainly suggestive. It should not be forgotten that hyperacidity occurs in gall-stones, chronic appendicitis and gastric neuroses; and that achylia may occur from chronic catarrhal or atrophic, gastritis, and as a functional condition. The chemical examination of the stomach contents is of value only when considered with symptoms and other laboratory findings; just as the presence of albumen in the urine does not make the diagnosis of nephritis positive without other examinations.

The Fasting Stomach.—The examination of the contents of the fasting stomach is quite important, in the diagnosis, prognosis and treatment of gastric diseases. The presence in the stomach of food eaten the previous day, before the patient has had breakfast, indicates serious organic stenosis (ulcer or carcinoma) or extreme atony and dilatation of the stomach. The presence of an excessive amount of gastric juice in the fasting stomach indicates gastro-succorrhea.

Blood.—The constant presence of blood in the stomach contents, unless the patient retches when the tube is introduced, is suggestive of ulcer or carcinoma.

Microscopic Examination of Stomach Contents.—The microscopic examination of the stomach is not of a great value in the examination of soldiers, though occasionally particles of ulcer or cancer tissue may be brought up through the tube, and the sarcinae and food remnants in the fasting stomach, indicates gastrecasis. The Boas-Oppler bacillus is found in the stomach contents in 90 per cent. of the cases of gastric carcinoma. This bacillus has also been found in the stomach contents, in which lactic acid was found, in cases of simple gastrecasis. Blood and pus cells are usually present in the stomach contents even in the early stages of gastric carcinoma.

The Feces.

Occult Blood.—Thorough examination of the feces should be a routine in every examination for digestive disease. The

presence of occult blood where there is no evidence of hemorrhoids, or ulceration of the rectum or colon, suggests a gastric or duodenal ulcer, or a carcinoma. It is important to exclude meat from the diet for several days before examination of the feces, particularly with the benzidin test. Repeated examination of the stools in ulcer and carcinoma will, in the great majority of cases, reveal occult blood, though its absence does not positively exclude either.

Intestinal Test Diets.—In suspected pancreatic disease, which is more frequent than is generally supposed in men from twenty to thirty years of age and in various intestinal disease, the Schmidt-Strasburger test diet with subsequent examination of the feces may be of value as in aid in diagnosis.

Microscopic Examination.—Microscopic examination of the feces is of little value in determining the degrees of digestion of various foods, except with the Schmidt-Strasburger test diet in intestinal and pancreatic diseases; but the question of intestinal parasites is an important one. It is hoped that much information regarding the prevalence, the geographic distribution and the life history of the various intestinal parasites will result from the systematic examination of the feces of soldiers drafted from various parts of the country.

X-Ray Examination.

The X-ray, while not infallible, is the most important aid in the diagnosis of gastro-intestinal disease. It gives information regarding the size, contour, position and muscular function of the stomach and intestines that can be obtained from no other source. It is, therefore, advisable in cases of suspected ulcer or carcinoma, or in gastroenteroptosis, or when the diagnosis is in doubt, for the patient to be given the benefit of an X-ray examination. The gastro-enterologist should endeavor to be present when fluoroscopic examinations of his patients are made. He should also go over the plates with the roentgenologist and should keep a record on his history blanks of all X-ray findings.

While fluoroscopic examinations give perhaps more information particularly in ulcer and carcinoma of the stomach, it is advisable to make one or more plates as a matter of record. In some cases the series of plates is best. The interpretation of roentgenoscopic and roentgenographic examination is of great

importance and caution must be exercised in making a diagnosis from the X-ray alone. When in doubt, it is best to make additional examination. In cases of gastric and duodenal ulcer that have been apparently cured, is worth while making plates a month or two, and six months, after the patient leaves the hospital, because it is important to get records of patients who have been cured.

Routine for Examination.

It is not possible to carry out a regular routine in the examination of every patient, but it is advisable to adopt a definite plan that can be followed in the majority of cases. With the acutely or severely ill patient, the examination and diagnosis should be made as quickly as possible, so that treatment may be begun without loss of time; but with the chronic cases like ulcer, gastretacis, chronic gastritis and other gastric disease and conditions, in which the patients not suffering acutely, several days will be required to complete the examination. In the latter class of cases, something like the following routine may be followed:

First Day.—Take the patient's history and make the physical examination. Weigh him and take temperature and blood pressure. A blood smear should be examined for malaria, and a differential count made on the first or second day in every case. An eosinophilia of over 5 per cent. is frequently the suggestion that leads to the positive diagnosis of uncinaria or other intestinal parasites. If the patient has fever, or if appendicitis or other acute inflammatory condition is suspected, a leucocyte count should be made at once, and repeated as often as necessary. If there are evidences of anemia, a red count should be made.

The full hospital diet, or the food that the patient is accustomed to eating, should be given, unless contra-indicated; and, in addition, at bed time, a ham or beef sandwich and three or four prunes, or a dozen raisins may be eaten as a test for motility.

No medicines, unless indicated for the relief of symptoms, are given on the first day. The reason that no medicines are prescribed should be explained to the patient, and if he is dissatisfied, a placebo, like 1 c.c. of tincture of gentian, may be given.

Second Day.—Gastric lavage at 7 or 8 A. M. The stomach tube should be introduced and the contents, if any, should be

removed by expression or aspiration. Then the stomach should be lavaged with 1 or 2 litres of plain warm water, the nurses or attendants can be taught to give this lavage. The macroscopic appearance (for blood, particles of food, pieces of the skin or prunes or raisins, etc.) should be noted; the chemical tests (for hydrochloric or lactic acid and blood) and microscopic examination for (meat shreds, starch granules, vegetable fibre, tissue shreds, blood, pus, sarcines, Oppler-Boas bacilli, and other bacteria) of the gastric contents, or of the sediments from the washings, should be made and the findings recorded.

At 8 A. M. Ewald or Dock test breakfast may be given, and the contents removed in one hour, and examined in the usual way.

Chemical (including tests for indican) and microscopic examination of the urine should be made, in every case, on the first and second day.

The first stool that the patient defecates after his entrance in the hospital should be examined macroscopically (for mucus, pus, connective tissue, muscle remnants, fats, potato and other vegetable remnants) chemically (for blood) and microscopically (for blood, pus, mucus, intestinal parasites, meat and vegetable fibres, fats and starch granules). The stools should be examined again on the second day and at the end of the week. If the benzidin or other test is positive for blood on the first examination the patient should be placed on a meat free diet for at least three days, and other specimens examined.

The stools may be kept in a container placed in a basin of warm water, or in an incubator to keep the specimen warm until it can be examined. A small tin bucket with a cover, which the patient may take to the toilet or latrine, is perhaps the best container for getting a specimen of feces. In some cases, when the stool cannot be obtained, a warm rectal tube may be introduced, and enough feces for microscopic examination will be caught in the open end.

It would be interesting to have a Wassermann in every case, and report the results at the end of a year. It should be made in every case in which the history of the patient, or his symptoms, indicate the possibility of luetic infection.

The Einhorn string test may be made on the first and second

nights, and, if positive, the strings should be kept in envelopes attached to the case history.

Third Day.—No breakfast, except a barium meal at 8 or 9 A. M., when the patient should be fluoroscoped and a plate made. In six hours there should be another fluoroscopic examination, and if there is retention of barium in the stomach, or other pathological finding, the second plate should be made.

If there is any suspicion of focal infection from the teeth, X-ray films should be made.

If not thought advisable before the third day, and there are indications of trouble with teeth, tonsils, lungs, heart, or other organs, the patient should be referred for consultation to the dentist, oto-laryngologist, tuberculosis or cardio-vascular specialist, neurologist, surgeons or other specialists on the hospital staff.

Fourth Day.—X-ray examination twenty-four hours after the barium meal, and repeated on the fifth day, if necessary. Other barium meals or enemata may be given if further X-ray examinations are thought necessary.

By direction of the Surgeon General.

ENDOCRINE FUNCTIONS AND THE DIGESTIVE APPARATUS.*

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The Relations between the endocrine glands and the digestive system may be classified under two main divisions, each of which, in its turn, falls under several heads.

I. *Relations of the Digestive Apparatus to Endocrine Organs Outside of Itself.*

A. Digestive Apparatus and the Thyroid Gland.
B. Digestive Apparatus and Parathyroid Glands.
C. Digestive Apparatus and Thymico-Lymphatic System.
D. Digestive Apparatus and Hypophysis Cerebri.
E. Digestive Apparatus and the Chromaffin System.
F. Digestive Apparatus and the Interrenal System.
G. Digestive Apparatus and the Gonads.
H. Digestive Apparatus and the Vegetative Nervous System.

II. *Internal Secretions Originating Within the Digestive Apparatus Itself.*

A. The Pancreatic Hormone.
B. The Duodeno-Jejunal Hormone (secretin).
C. The Hormone of the Pyloric Glands (gastrin).
D. Hepatic Products (antithrombin; ures; glucose).

I. *Relations of the Digestive Apparatus to Endocrine Glands Outside Itself.*

A. The Digestive Apparatus and the Thyroid Gland.

Symptoms referable to the digestive system and the thyropathies may be arranged in three groups:—

(*a*) Symptoms referable to the digestive apparatus in Graves' disease.

*Read at the annual meeting of the American Gastro-Enterological Association, May 7th, 1918.

(*b*) Symptoms referable to the digestive apparatus in myxedema of children and of adults.

(*c*) Influence of the quality and quantity of food ingested upon the function of the thyroid gland.

Each of these groups, in its turn, falls under several different headings:—

(*a*) *Symptoms Referable to the Digestive Apparatus in Graves' Disease.*

These include: (1) Disturbance of salivary secretion; (2) disturbance of appetite; (3) disturbance of gastric secretion and motility; (4) disturbance of intestinal secretion, especially unmotived diarrhea and spastic constipation; and (5) disturbance of carbohydrate metabolism.

(1) *Disturbance of Salivary Secretion.*—Careful research has failed to detect any hormone formed by the salivary glands. Disturbance of the salivary secretion in Graves' disease usually takes the form of dryness of the mouth, due to a diminished flow of saliva, but occasionally, though rarely, the flow is increased. Sattler considers that the latter symptom is analogous to the increase of secretion in the lachrymal glands observed in some cases of Graves' disease and that it is associated with disturbance of the glosso-pharyngeal nerve.

(2) *Disturbance of Appetite.*—In the majority of cases of Graves' disease the appetite, especially in the early stages, is increased and there is often polyphagia. Later on, the appetite may become less and in some cases there is absolute anorexia.

(3) *Disturbance of Gastric Secretion and Motility.*—In Graves' disease the gastric secretion, as a rule, is diminshed, but there are certain cases in which it is increased, and crises of hyperacidity may occur. Attacks of vomiting, due to the disturbance of gastric motility, are not infrequent. According to Sattler, they are present in about 15 per cent. of cases. The vomiting usually occurs in paroxysms, generally without relation to food and often without nausea. It may be quite uncontrollable, taking place as often as thirty times during one day. When the attack is over, there may follow a period of increased ingestion of food.

(4) *Disturbance of the Intestinal Function.*—Attacks of watery, unmotived diarrhea, varying in frequency from 4 to 30

stools a day, are quite common in Graves' disease. Sattler states that they are present in 30 per cent. of cases. The diarrhea is not accompanied by pain, but in certain rare cases blood has been observed in the stools. Möbius regarded this diarrhea as an effort to cast out the gland substance that is circulating through the body. Eppinger and Hess believe it to be an expression of vagotony, but Falta is inclined to disagree with this view on the ground that vagotonia is more apt to be accompanied by spastic constipation. In some cases of Graves' disease spastic constipation alternates with attacks of diarrhea that stop just as suddenly and, apparently, as causelessly, as they began.

(5) *Disturbance of Carbohydrate Metabolism.*—Rapid emaciation is a marked feature of Graves' disease, though the patients often have good appetites and eat abundantly. The explanation of this paradox has been found in the acceleration of metabolism incident to the condition. All the metabolic processes of the body, including the total combustion (calories, carbohydrates, protein, fat, and mineral-metabolism) are appreciably accelerated, the thyroid secretion acting apparently as a fan to the fires of the body. Slight elevations of body temperature are sometimes observed in Graves' disease and these, when not due to some inter-current infection, in all probability indicate disturbance of the heat-regulating mechanism, overtaxed by accelerated oxidation. In severe cases a cachexia may develop, due to increased disintegration of protein and consequent difficulty in maintaining a nitrogenous equilibrium. As regards mineral metabolism, an excess of phosphorus is often lost through the intestine and the output of calcium in the feces is increased. Sometimes the emaciation progresses in a uniform manner; sometimes it is subject to acute exacerbations, called by Huchard *"crises d'amaigressement."* Its extent is generally in proportion to the severity of the disease. When vomiting and diarrhea are present, the loss of weight is proportionately rapid.

(*b*) *Symptoms Referable to the Digestive Apparatus in Myxedema of Children and of Adults.*

These include: (1) Disturbance of salivary secretion; (2) disturbance of appetite; (3) disturbance of dentition; (4) disturbance of gastric secretion and motility; (5) disturbance of intestinal secretion and motility; and (6) disturbance of metabolism.

(1) *Disturbance of Salivary Secretion.*—Myxedema and myxedematous conditions are characterized by a diminution of the excitability of the entire vegetative system, the effect of which is to reduce the activity of all the secretory organs. The mucous membrane of the mouth is dry, the salivary secretion being thick and viscid, as well as more or less diminished in amount. The tongue is often increased in volume, so that it is visible between the teeth and shows the impression made by them. Stevenson and Halliburton assert that they have found the mucin content of the salivary glands increased in thyroid insufficiency. Their observations, however, have been contested by other investigators.

(2) *Disturbance of Appetite.*—The appetite in thyroid insufficiency is usually diminished and when the inadequacy is severe, there is complete anorexia. Hertoghe states that meat is peculiarly distasteful.

(3) *Disturbance of Dentition.*—In adults suffering from myxedema or myxedematous conditions the teeth are almost always in a bad condition. They decay rapidly and are very liable to fall out. The gums are red and inflamed, with a tendency to recede. Hertoghe notes that at the level of the dental interstices the gums are continued in polypiform prolongations. Falta reports a case in which during the course of one year, the crowns of the teeth became so completely worn off that the teeth were reduced to about one-half their natural length. The incisors consisted only of short stumps, provided with broad grinding surfaces. In children suffering from myxedema dentition is delayed and when the milk teeth finally make their appearance, they are apt to be permanently retained, though rudiments of the other teeth are sometimes present as well.

(4) *Disturbance of Gastric Secretion and Motility.*—The gastric secretion, like all the others, is reduced in amount and the acidity is apt to be diminished. In one case under my own observation examination of the stomach juice showed a complete absence of free HCl, indeed this state of things, together with pigmentation of the skin and pronounced anemia, were so marked as to suggest an atrophic gastritis or a developing carcinoma ventriculi.

(5) *Disturbance of Intestinal Secretion and Motility.*—Atony of the intestines, with constipation of a peculiarly intractable character, is an outspoken feature of myxedema. Myxedematous

patients will sometimes go for five, ten, or even as much as twenty-five days without an action of the bowels. Hertoghe believes this atonic condition is largely due to infiltration of the gastro-intestinal walls with mucin. Falta considers the chief factor in it to be the decreased tonus of the vegetative nervous system, inducing persistent paresis, that, in its turn, leads to retention of waste material, with resulting toxemia, reacting upon the already enfeebled thyroid gland. When the abdominal walls are weak, there may be more or less downward displacement of the stomach and intestines, with formation of adhesions. Hertoghe considers that in such cases there is a noticeable tendency to appendicitis, but he is uncertain whether it should be attributed to habitual overloading of the intestines with consequent ptosis and the formation of adhesions, whereby the appendix loses its motility and becomes fixed in a bad position, or to inflammation of its mucous membrane due to invasion by the lymphoid corpuscles of the appendix. He, himself, inclines to the latter view, because he has observed that phlegmasia of other lymphoid organs, such as the tonsils, is frequently observed in thyroid insufficiency, and he is of opinion that an association must exist between inflammation of the tonsils and inflammation of the appendix. In children suffering from congenital myxedema the abdomen is apt to be tympanitic and may be distinctly pot-bellied. Umbilical hernia is sometimes observed and prolapse of the rectum is not uncommon. In adults, thyroid insufficiency is sometimes accompanied by rectal hemorrhage, which has been thought to be due partly to the aging of the rectal veins and partly to defective coagulation of the blood. Hemorrhoids are quite common.

(6) *Disturbances of Carbohydrate Metabolism.*—The changes in metabolism accompanying myxedema, as we should expect, are diametrically opposed to those present in Graves' disease. All the metabolic processes are slowed, and it follows that increase in weight rather than emaciation is an outspoken feature of the disease, in spite of the fact that patients suffering from thyroid insufficiency have poor appetites and may eat very little. The total metabolism (calories) is much less than normal and the oxygen used may be reduced from 50 to 60 per cent. Protein metabolism also is slowed and the total amounts of nitrogen, of urea, and of uric acid eliminated are all less than normal. Car-

bohydrate tolerance is markedly increased, no alimentary glucosuria appearing after the ingestion of 200 to 300 grm., of d-glucose. As regards mineral metabolism the results of investigation are conflicting.

(c) *Influence of the Quantity and Quality of Food Ingested Upon the Function of the Thyroid Gland.*

Very little is known concerning the influence of food upon thyroid function, as regards either quantity or quality. The subject is one that will repay further investigation. Some facts, however, have been collected, bearing upon iodine, oatmeal, protein, and acetonitril.

Iodine.—Iodine is found in many of the organs of the body, but the iodine content of the thyroid gland is much larger than that of other organs relatively rich in it. According to Magnus Levy, the normal content of the thyroid gland is about 0.3 to 0.9 mgrm. of iodine for one kgrm. of dried thyroid substance. In the fetus and also in new-born babies the thyroid is iodine-free. The activity of the thyroid gland is bound up with its iodine content, and the symptoms appearing after extirpation of the gland may be alleviated by administration of its substance. All experience points to the fact that the thyroid carries iodine in a special combination. In this connection, the chemical studies of Kendall of the Mayo clinic assume a special interest. The functions of the normal thyroid may be influenced by the administration of iodine. Falta states that the thyroid of the dog can be made extremely poor in iodine by an abundant meat diet, a fact pointing to a rapid leading off of the thyroid substance. Kocher, in 1905, found that in the purely parenchymatous form of Graves' disease, when the parenchyma is functioning abundantly, more iodine is excreted than is introduced into the body, so that the thyroid tissue is, as it were, "melted down" and symptoms of thyroidism may appear. In the colloid form of Graves' disease, on the other hand, he asserts that the iodine content is not absolutely greater than it is in the normal gland, while, relatively it is less. One of the most recent theories regarding iodine in the thyroid is that albuminous substances, having a toxic reaction, are absorbed from alimentary canal and then rendered non-toxic in the thyroid by iodinization. But this theory is little more than speculation.

Oatmeal.—Some observers believe that the ingested oatmeal will augment the activity of the thyroid gland. They advise that the use of oatmeal be discouraged in Graves' disease.

Proteins.—The pancreas and the chromaffin tissue govern carbohydrate metabolism, whereas the thyroid gland is more especialy concerned in protein metabolism. In hyperthyroidism protein metabolism is distinctly accelerated, and the patients require more protein and more protein-sparing carbohydrates, in order to maintain themselves in nitrogen metabolism. It does not seem to be fully determined whether the increase of protein-exchange in over-activity of the thyriod is primary or only the result of increased metabolism of carbohydrates and fat. In hypothyroidism, the protein-exchange, as we should expect, is low, and the protein requirement light. It has been noted that the symptoms of under-activity, following extirpation of the thyroid, are aggravated by a meat diet, but Dale calls attention to the fact that these observations were made before the significance of the parathyroid glands in connection with strumectomy was recognized.

Acetonitril.—Within recent years some interesting experiments have been made by Reid Hunt, showing that when a white mouse was fed with blood from a patient suffering with Graves' disease, it always developed an increased resistance to acetonitril intoxication, while the blood of a normal individual, used as a control, had no such effect. This observation supplies additional evidence that the thyroid gland possesses an internal secretion that is essential to normal growth and metabolism. It also furnishes a diagnostic test that may prove to be clinically useful.

B. Digestive Apparatus and the Parathyroid Glands.

The physiological significance of the parathyroids was first demonstrated, in 1891, by Gley, who believed that they could assume the function of the thyroid gland after its extirpation. The results of their total removal or insufficiency are better known to us than the effects of removal or insufficiency of any other endocrine glands. Concerning their over-activity, however, we know little or nothing. The clinical symptoms of tetany were first described by Trousseau in 1851 and the name, tetany, was given to the syndrome in question by Corvisart in 1852. At that time clinicians recognized only that various disturbances

of the digestive tract, such as cholelithiasis, pyloric stenosis, and carcinoma ventriculi, were frequently accompanied by this syndrome, but of late years the doctrine of a special hormone concerned in the causation of tetany has gained adherents and at present evidence favors the view that the hormone in question acts chiefly upon the higher neurons in the central nervous system.

The digestive symptoms associated with over- or under-function of the parathyroids may be classified as follows:—

(*a*) Enamel defects in parathyroid insufficiency.

(*b*) Calcium excretion in parathyroid insufficiency.

(*c*) Gastric tetany.

(*d*) Barker and Estes syndrome.

(*e*) Disturbance of salivation in tetany.

(*f*) Spasm of the smooth muscle fibres of the gastro-intestinal tract in tetany.

(*a*) *Enamel Defects in Parathyroid Insufficiency.*—When tetany occurs in childhood, the enamel of the teeth does not develop properly and we know now that this defective development is not due to rachitis, as was at first supposed. In tetany there is always hypoplasia of the enamel, leading to the formation of horizontal furrows, as well as to hole-like defects. The incisors and canines are most often affected; the molars more rarely. When the tetany undergoes frequent exacerbations, parallel lines may be seen running along the teeth, one below another, corresponding to the periods of increased severity. Speigler has reported a case of recurrent tetany, in which there was an attack every spring for eight years, beginning at the end of the second year of life. All the teeth whose crowns must have been formed at the time of the first attack were normal, whereas those whose crowns developed later showed enamel defects. Erdheim has observed similar disturbances of the enamel formation in experiments upon rats, opaque spots forming on the anterior surface of the incisors and advancing toward the point of the tooth with its growth, until sooner or later, the tooth breaks off or else the defect in the enamel heals, leaving a shallow groove.

(*b*) *Calcium Excretion in the Feces in Parathyroid Insufficiency.*—In both human and experimental tetany there is increased elimination of calcium. The relations between parathyroid insufficiency and calcium metabolism, though not, as yet,

fully understood, form the basis of the treatment of tetany by means of calcium salts. MacCallum and Vögtlin found that the administration of a 5 per cent. solution of calcium acetate and calcium lactate, given orally, intravenously, or subcutaneously, to dogs whose parathyroids had been removed, was followed by the disappearance of the tetanic symptoms. The convulsions recurred at the end of twenty-four hours, but they could be again subdued by a repetition of the treatment. These results, together with some other similar ones, induced MacCallum and Vögtlin to conclude that the parathyroids are actively engaged in controlling the metabolism of calcium in the body.

(*c*) *Gastric Tetany.*—Disturbances of the stomach and intestines of varying intensity, are present in many cases of tetany. This class of cases can be divided into two groups: one where tetany develops in persons who have already suffered for some time with gastric disturbance; the other, where the gastro-intestinal trouble occurs at, or immediately after the outbreak of tetany. Patients belonging to the second group of cases manifest hyper-excitability on the administration of pilocarpine, with relaxation of stomach tonus, an increase of gastric secretion, and pronounced stasis, leading eventually to tenesmus and diarrhea. It is possible that the diarrhea often present in tetany may depend upon this increased secretion by the gastro-intestinal mucosa. There are several sub-groups of gastric tetany, each characterized by some specific feature or features. In one of these, the symptoms associated with the digestive system constitute only one indication of the tetanic state. In another, indisposition of the stomach and intestine may be simply the determining factor in the development of the tetany. Kussmaul has called attention to one particular form, in which the digestive disturbance has existed for a long time; the most varied conditions, such as hour-glass stomach, or cicatricial ulceration of the duodenum, have been found to accompany it. Cases of dilatation of the stomach without demonstrable stenosis have also been reported. Numerous hypotheses have been advanced to explain the gastric stenosis and dilatation observed in tetany. According to one theory there is a pre-existing gastric dilatation, during which the tetany develops. According to another view, the dilatation is due to an atonic condition caused by stagnation of the gastro-intestinal contents. In favor of the latter theory it may be said

that in many cases the tetanic symptoms disappear promptly when the stomach is washed out. It has also been suggested that the tetany may be due to a thickening of the blood caused by frequent vomiting and diminished absorption of water.

(*d*) *Barker and Estes Syndrome.*—This is a remarkable condition in which chronic dilatation of the upper part of the gastro-intestinal tract occurs, accompanied by tetany and hematoporphyrinuria. With Dr. W. L. Estes, Jr., I have described an interesting family in which chronic dilatation of the stomach and duodenum occurred in three sisters, one of whom developed a polyneuritis associated with tetaniod attacks.

(*e*) *Disturbance of Salivation in Tetany.*—One of the characteristic features of tetany is an increased sensitiveness to pilocarpine, resulting in a marked excretion of saliva. Spontaneous disturbance of the salivary secretion is not common, but sialorrhea occasionally occurs.

(*f*) *Spasm of Smooth Muscle Fibres in the Gastro-Intestinal Tract in Tetany.*—Spasm and contraction of the smooth muscle fibres of the intestinal tract, due to increased tonus in the vegetative nervous system, are sometimes seen in tetany. Pyloric spasm, leading to acute dilatation of the stomach, sometimes occurs during the acute stage. Falta has reported a case in which an X-ray examination made during an acute exacerbation of tetany, showed the stomach to be small, much contracted, and divided into two parts, indicating a complete spasm of the longitudinal musculature. There was also insufficiency of the pylorus. This phenomenon continued to recur with each exacerbation, but it gradually decreased in intensity, as the tetanic condition improved, and an X-ray examination made after recovery showed the stomach to be perfectly normal. Falta has also seen this kind of spasm associated with vomiting and disturbance of the bowels in animals deprived of the parathyroids. These observations point to the fact that in the acute stage of tetany the gastro-intestinal tract may show signs of exaggerated excitability and heightened tonus, increasing up to a definitely spasmodic condition, accompanied by increased secretion. Ibrahim has observed severe gaseous distention of the abdomen in such patients, due, as he believes, to the sphincter ani being involved in the tetanic spasm. The bronchospasm, sometimes seen in tetany, may be due to changes in the tonus of the smooth musculature

of the bronchi, but it is possible that spasm of the diaphragm and of the respiratory muscles play some part in its causation. Bouveret and Devic have described one special form of gastric tetany accompanied by paresthesia and typical spasm of the extremities that may lead to death from asphyxia, chiefly through the involvement of the respiratory muscles.

C. The Digestive Apparatus and the Thymicolymphatic System.

The thymus gland was formerly regarded as part of the general lymphatic system, but it is now recognized as belonging also to the great group of glands furnishing internal secretions. At present clinicians are trying to establish definite symptoms associated with over- and under-function of the thymus as has been done for the other endocrine glands. Disturbances of the thymico-lymphatic system are generally associated with more or less hyperplasia of the thymus gland, manifesting itself, as far as the digestive system is concerned, especially from three standpoints: (*a*) Hyperplasia of the tonsils and of the lymphatic nodules in the digestive tract; (*b*) abnormally long intestine; (*c*) large medial incisors.

(*a*) *Hyperplasia of the Tonsils and of the Lymphatic Nodules in the Digestive Tract.*—In outspoken cases of status lymphaticus there is always hyperplasia of the lymphatic system. This may be expressed by enlargement of the tonsils, of the follicles at the base of the tongue, of the pharyngeal lymphatic ring, and, as regards the intestine, especially, of Peyer's patches and the salivary follicles.

(*b*) *Abnormally Long Intestine.*—Autopsies made upon patients who have exhibited a status thymico-lymphaticus during life have in a number of instances revealed the presence of an abnormally long intestine.

(*e*) *Large Medial Incisor Teeth.*—I have frequently been struck with the very large size of the uper medial incisor teeth in patients with status thymico-lymphaticus. An examination of the literature reveals the fact that this finding is a common one.

D. Digestive Apparatus and the Hypophysis Cerebri.

The symptoms associated with disturbance of the hypophysis, as with the other endocrine glands, may arise from over- or from

under-activity. In many cases, however, the function is so perverted that symptoms attributable to over-action may be combined with those due to under-action, resulting in the condition known as dyshpophysism or dyspituitarism. The digestive disturbances associated with these perversions of function may be discussed from the following standpoints: (*a*) The hypophysis and splanchnomegaly; (*b*) thirst in diabetes insipidus; (*c*) effect of pituitrin upon the smooth muscle walls of the intestine, and (*d*) the hypophysis and carbohydrate metabolism.

(*a*) *The Hypophysis and Splanchnomegaly.*—Over-secretion of the anterior lobe of the pituitary gland is associated with hypertrophic changes in both the hard and the soft tissues of the body. In the digestive tract the effect upon the hard tissues may be seen in the teeth, which though they do not change in size, become farther and farther apart, owing to enlargement of the jaws, finally becoming what are now commonly known as "hag's teeth." The hypertrophic changes in the soft tissues take the form of a general splanchnomegaly. In the digestive tract this is first seen in a thickening of the tongue, the lips, and the mucous membrane lining the oral cavity. The tongue sometimes increases in size to such an extent that, in spite of the enlargement of the jaws, it projects over the teeth. This thickening of the tongue may be so great as to affect articulation. Enlargement of the walls of the stomach and intestine is sometimes observed as well as enlargement of the liver, pancreas, and spleen. In some cases the enlargement of the liver is only the sequel of a cardiac insufficiency; in others it is a partial manifestation of a true splanchnomegaly. Enlargement of the spleen is associated with enlargement of the general lymphatic apparatus. Dilatation of the stomach has been found with the polyphagia so often associated with acromegaly. The length of the small intestine is increased, and Cunningham has reported a case in which it was doubled. In many cases of acromegalic gigantism, the pancreas has been found to be of enormous size (270 grm. in one instance), but in other conditions associated with hyperpituitarism, it may be of normal size, or it may be sclerotic.

(*b*) *Thirst in Diabetes Insipidus.*—The two most striking symptoms of diabetes insipidus are polydipsia and polyuria, but contrary to what we should expect, the polydipsia leads neither to heart hypertrophy nor to arterial hypertension. As long as

sufficient water is taken in, the daily output of solids, as estimated by the urine, remains normal. Experiments upon animals have recently shown that the ability of the kidneys to secrete a concentrated urine depends upon a product of secretion of the pars intermedia of the hypophysis. In cases of diabetes insipidus in human beings, symptoms pointing to involvement of the hypophysis cerebri are frequently present. The quantity of urine excreted in human diabetes insipidus can be controlled by the hypodermic administration of pituitrin or of pituitary liquid. This is clear from a number of cases reported in the literature. In association with Dr. Mosenthal I reported such a case a year ago; recently with Dr. Hodge I have reported a second similar case. The tendency at present, therefore, is to look upon idiopathic diabetes insipidus as one of the diseases of the glands of internal secretion.

(*c*) *Effect of Pituitrin Upon the Smooth Muscle Fibres of Intestinal Wall.*—Bell, in 1909, called attention to the power possessed by the extract of the pituitary gland to restore peristalsis to the paralytically distended bowel. In 1900, Beyer and Peter found that after a preliminary diminution, both rhythm and tone were strikingly increased, the rhythmic movement sometimes as much as tenfold. They consider the preliminary phase to be due to stimulation of the sympathetic fibres inhibiting the muscles; the second phase, in their opinion, is due to stimulation of Auerbach's plexus and of the post-ganglionic fibres. They believe, therefore, that they have been able to distinguish two different substances, each of which has a direct action upon the intestine. Pancoast and Hopkins have recently observed the effect of pituitrin upon the gastro-intestinal tract in a series of eleven patients. Their method was to inject pituitrin intravenously and observe its effect upon the alimentary canal by means of a series of X-ray plates, taken at intervals during digestion. The results were decidedly variable, but there was sufficient uniformity to convince them that the primary effect upon the stomach was, as a rule, a decrease in motility, followed by an increase. In the small intestine, motility was, in general, unaffected, but occasionally it was increased. Upon the large intestine the extract had no effect whatever.

(*d*) *The Hypophysis and Carbohydrate Metabolism.*—It

seems probable that the pars intermedia exercises some control over carbohydrate metabolism, as evidenced by:—

(1) Glycosuria in acromegaly.

(2) Obesity in dystrophia adiposo-genitalis.

(1) *Glycosuria in Acromegaly.*—The condition known as acromegaly is due to a hyperfunction of the hypophysis cerebri. Though the bony changes are due to hyperfunction of the anterior lobe, the disease is frequently complicated with glycosuria or with diabetes mellitus, due, in all probability, to excessive secretion of the posterior lobe. In some instances, the glycosuria appears only during the initial stage of the disease and later on these cases show a marked carbohydrate tolerance. Cushing has reported several cases of this nature. The diabetes associated with acromegaly may follow the usual course, ending in coma and death, but, as von Noorden has pointed out, in not a few cases, the glycosuria shows a striking independence of the sugar value of the diet.

(2) *Obesity in Dystrophia Adiposo-Genitalis.*—The condition known as dystrophia adiposo-genitalis is characterized by quickly developing obesity, infantilism of the genitalia, and myzedema-like changes in the skin. These symptoms were first clearly described by Fröhlich in 1901 and are now known as Fröhlich's syndrome. As a rule, the condition is associated with a tumor or some other disturbance of the hypophysis that induces a decrease in its functional activity, especially in that of the posterior lobe. The accumulation of fat, which is the most prominent symptom, is situated largely about the abdomen and thighs, but it may be more generally distributed. In the more severe forms of the disease, thick pads of fat may develop in the supra- and infra-clavicular regions. Some authorities refer the obesity directly to a loss of functional activity of the hypophysis; others believe it to be secretory in its nature, dependent upon functional disturbance of the sex glands, and manifesting itself in faulty development of the genitalia. Falta considers that the latter view is established by the fact that although there may be no obesity proper, the abnormal distribution of fat, confined to certain localities, is always present, even in cachectic and markedly emaciated individuals. There has also been some difference of opinion as to whether the decrease in functional activity is in the anterior lobe, the posterior lobe of the hypophysis,

or both. At present, the evidence points to the anterior lobe as being the part of the gland chiefly involved, though the whole gland may be at fault. Clinical observation would seem to indicate that the obesity in hypophyseal dystrophy is associated with disturbances of carbohydrate metabolism, but investigations upon this subject are, as yet, scanty and imperfect. One point clearly established, however, is that the changes in carbohydrate metabolism are in marked opposition to those in acromegaly. In acromegaly carbohydrate tolerance is more or less reduced and glycosuria is of frequent occurrence. In hypophyseal dystrophy, on the other hand, there is an abnormally high tolerance of carbohydrates with no tendency to glycosuria.

E. The Digestive Apparatus and the Chromaffin System.

Our knowledge of the chromaffin system is of very recent growth, being mainly a product of the last few years. Magendie, in 1841 told his students: "I have nothing to say on the suprarenal capsules. Since nobody any longer belongs in *atra bilis,* the capsules have ceased to be a secreting organ." At present we know that the chief function of the chromaffin system (including the medulla of the suprarenals) seems to be the production of adrenalin and the continuous supply of that substance, sometimes described as a sympathetic hormone, to the blood. The action of adrenalin upon the digestive tract may be considered under three heads: (*a*) Adrenalin and the smooth musculature of the gastro-intestinal tract; (*b*) adrenalin and glucose metabolism; and (*c*) adrenalin and ulceration of the stomach and intestine.

(*a*) *Adrenalin and the Smooth Musculature of the Gastro-Intestinal Tract.*—Adrenalin is a specific product of the chromaffin cells, that is to say of cells belonging essentially to the true sympathetic system. When it is injected into the blood-vessels it stimulates the termination of the sympathetic fibres in the glands and the visceral muscles, its action being restricted apparently to these terminations. When it is injected in doses too small to cause a rise of blood-pressure, it acts upon the smooth muscles of the gastro-intestinal tract, inhibiting peristalsis and stimulating contraction of the sphincters. Hoskins and McClure have found, however, that in extremely minute doses, it actually increases peristalsis.

(*b*) *Adrenalin and Glucose Mobilization.*—When adrenalin is administered, whether subcutaneously, intravenously, or by

intra-peritoneal injection, it increases the amount of sugar in the blood and sugar makes its appearance in the urine. Herter and Wakeman stated that this effect was most marked when the adrenalin was applied directly to the pancreas and they attributed it to toxic action of the adrenalin preventing the formation of the internal secretion in the pancreas by which the mobilization of sugar in the liver is controlled. In Nöel Paton's opinion the glycosuria and the increased glycemia are due to the action of adrenalin upon the sympathetic fibres in the liver, which is, of course, the storehouse for carbohydrates. It contains a rich nerve plexus, an extension of the splanchnic nerves, formed by a migration of neurons from the wall of the intestine. Stimulation of these neurons is known to cause an increased conversion of glycogen into glucose. It has also been shown that stimulation of the central end of the vagus causes glycosuria, even after removal of the suprarenal glands. There seems to be no doubt, however, that the liver is supplied by true sympathetic fibres and that stimulation of these fibres, either directly or reflexly, causes the mobilization of sugar. The fact, first stated by Elliott, and now known as *Elliott's law,* that adrenalin acts by stimulating the endings of the true sympathetic nerves, seems to be of general application, and under its working, it would seem probable that the adrenalin stimulates these endings in the liver, thus producing an output of sugar.

(*c*) *Adrenalin and Ulceration of the Stomach and Duodenum.*—Gibelli in 1909 and Finzi in 1913 called attention to the facts that animals dying after removal of both adrenals were found, in a number of cases, to have ulceration of the gastric mucosa. Finzi also showed that if, after the adrenals were removed, adrenalin was injected into the circulation, the gastric mucosa remained intact. These facts have since been confirmed by other observers. Mann, in 1915, performed some experiments in which he showed that the ulcers formed after removal of the suprarenals are apparently peptic ulcers, forming at the site of local hemorrhage in the gastric mucosa and usually penetrating to the muscularis mucosa, with complete loss of epithelium They appear to develop only in an acid medium, but some further experiments of Mann's seem to indicate that the acid plays only a secondary part in their production.

A year later Friedmann published the results of some ex-

periments, both clinical and experimental, as to the causation of gastric ulcer in general, which had led him to conclude that such ulcers are due to functional disturbance of the nerves supplying the areas involved, and that this disturbance arises from errors of internal secretion. His arguments are: First, that patients suffering from chronic peptic ulcer, in whom the nervous element was well marked, were not usually benefited by operation, and if such patients were questioned closely, a number of the stigmata accompanying disturbance of the vegetative system were found to be present. Second, that patients under his own care, who were suffering from gastric ulcer, presented vagotonic symptoms and responded readily to the pilocarpine test, whereas those suffering from duodenal ulcer showed sympathetic symptoms and reacted more readily to adrenalin. Third, that experiments carried out under his direction, showed a disturbance in the percentage of blood sugar in patients with gastric ulcer that he believed to be connected with the secretion of the adrenal glands. Friedmann, therefore, adopted as a working hypothesis, the view that the initial stage of duodenal ulcer may be caused by excessive secretion of the adrenals. He administered adrenalin to dogs intravenously, subcutaneously, and intramuscularly for about two weeks, in doses not exceeding three mgrms. of the commercial solution (1:1000). In 11 dogs out of 12, "lesions, erosions, or superficial ulcerations" were found in the duodenum, with only occasional gross changes in other organs. In normal dogs, used as controls, the gastric and duodenal mucosa was intact. He also found that after one-sided thyroidectomy in dogs and in rabbits "lesions or ulcers" were present in the stomach and intestines, most frequently in the stomach. This observation agrees with the fact, mentioned incidentally by Carlson and Jacobson, that they found gastric and intestinal lesions in 75 per cent. of thyrodectomized dogs.

From these results Friedmann considers it probable that the gastric lesions in question may be dependent upon adrenal insufficiency, as well as upon excess of adrenalin. They may also, in his opinion, depend upon the alternating effects of hyper- and hypo-function of the adrenals. A correlation of the thyroid and adrenal secretions would also seem to be suggested. He has seen several cases of Graves' disease accompanied by the symptoms of peptic ulcer, and two of his patients who were operated

on for it, developed peptic ulcer later on. In conclusion, he remarks that, if his theory is correct, the increasing frequency of peptic ulcer may well be due to disturbances of the vegetative system, arising from the haste and high tension that characterize our present modes of life, and exciting disturbances of the endocrine glands.

During the last year several short reports have appeared of experiments confirming the presence of an association between gastric and duodenal ulcer and disturbance of the adrenals.

F. Digestive Apparatus and the Interrenal System.

The cortex of the suprarenal glands and certain similar tissues does not belong to the chromaffin system, but to the so-called interrenal system. In the lower animals the interrenal organs remain permanently separated from the chromaffin system, but in human beings the interrenal system disappears, except for the cortex of the suprarenal glands, though a few minute masses, the size of a pinhead may be found scattered through various localities in the vicinity of the adrenal glands. Digestive symptoms are a prominent feature in the abnormal condition of the adrenal and the interrenal systems, known as Addison's disease, that arises from the combination of congenital inferiority of these systems with acquired injury to them, especially tuberculosis and syphilis. These symptoms are: a small and capricious appetite with a sensation of fulness after eating, hiccough, and eructations, leading eventually to complete anorexia, nausea, and vomiting. Constipation is present at the beginning, but as the disease progresses, it is characterized by attacks of diarrhea. Epigastric pain, both diffuse and localized, is often present, with rigidity of the abdominal muscles, and, it may be, pain in the lumbar or sacral regions. The epigastric pain may be paroxysmal in character, suggesting gastric crises, especially as remissions and exacerbations are features of the disease in the beginning. At a late stage the vomiting is often persistent and severe. The vomited material may contain mucus and bile with traces of blood. Examination of the stomach contents usually reveals no marked abnormality up to an advanced stage of the disease. Then the HCl may be reduced in amount or altogether wanting, and there may be diminution of peristalsis with undue excitability of the mucous membrane. The stomach and intestines frequently show congestion of the

mucous membrane as well as ecchymoses. Peyer's patches and the lymphoid tissue generally along the intestinal tract are sometimes found to be ulcerated.

G. Digestive Apparatus and the Gonads.

Changes in the internal secretion of the sexual glands, or gonads, are closely associated with disturbance of carbohydrate metabolism, and are manifested in two ways—namely, by (*a*) increased carbohydrate tolerance at the menopause; and (*b*) increased carbohydrate tolerance in eunuchoidism and eunuchism.

(*a*) *Carbohydrate Tolerance at the Menopause.*—At the menopause ovulation ceases entirely and the ovaries show retrogressive changes in general. Their endocrine function, however, retains some portion of its activity. In from 42 to 52 per cent. of cases of suppression of sexual activity is accompanied by an increased deposit of fat, but, as Biedl observes, it is sometimes difficult to distinguish between obesity of genital origin and that due to changes in the hypophysis.

(*b*) *Carbohydrate Tolerance in Eunuchism and Eunuchoidism.*—As Biedl observes, the fact that castration leads to increased deposition of fat is one of the oldest pieces of human knowledge. In true eunuchs, that is to say, men in whom the sexual glands have been removed by operation, metabolism is affected as it is in women at the menopause. In regard to obesity eunuchs are of two types. Those belonging to one type are tall and relatively thin; those belonging to the other are fat and pudgy-looking with broad hips and accumulations of fat in the buttocks and over the trochanters and the crests of the ilia. Even the thin eunuchs exhibit unusual deposits of fat in the lower abdomen and buttocks. In order to determine the nature of the change in nutritional conditions after castration, as well as to ascertain the cause of the abnormal deposit of fat, Löwy and Richter estimated the total metabolism (*i. e.,* intake of oxygen and excretion of carbon-dioxide) in castrated dogs of both sexes and found that metabolism was reduced and that this reduction was maintained for months and even years. From these results they concluded that the reduction of metabolism after castration is due to a diminution of the processes of metabolism and that the obesity is not necessarily degenerative. Experiments made in regard to the influence of the sexual glands upon protein metab-

olism show that castration does not lead to changes in it at any period of life, and that the increased excretion of nitrogen observed by certain workers after the exhibition of ovarian substance was due to increased ingestion of food containing protein. The increase in general metabolism following the administration of ovarian substance would seem to be entirely due to the decomposition of non-nitrogenous substances.

Eunuchoidism, that is to say, the condition in which persons, without being castrated, simulate the manifestations belonging to the true eunuchs, is often accompanied by disturbance of carbohydrate metabolism. Though the eunuchoid condition depends largely upon a hypogenitalism, the other glands of internal secretion are simultaneously involved, to a greater or less extent, so that some authorities include eunuchoidism among the so-called multiglandular syndromes. In all such cases there is an abnormal deposit of fat and a test for alimentary glycosuria shows that the limit of carbohydrate tolerance must be high.

H. Digestive Apparatus and the Vegetative System.

The vegetative system may be considered under two heads: the *sympathetic* and the *cranio-sacral* (vagal) system. Taken together these are called by Langley the *autonomic system.* These two systems are antagonistic, and under normal conditions a sort of balance is kept up between them by the chemical action of hormones upon their nerve cells. As Meltzer has observed, "everywhere where excitation is, is also present inhibition." In the smooth muscle fibres of the gastro-intestinal tract, for example, contraction is stimulated by the N. vagus and inhibited by the N. sympathicus.

There is a close relation between the endocrine glands and the vegetative nervous system. Both the sympathetic and the vagal systems are stimulated by the internal secretion of the thyroid and the tonus of both systems is closely related to the thyroid function. In acromegaly also this tonus may be either increased or diminished, so that it would seem that the internal secretion of the hypophysis has a direct effect upon the vegetative system. Some of the symptoms connected with it in acromegaly, however, are doubtless due to the secondary influence of other endocrine glands. The continuous supply of adrenalin

poured out by the chromaffin system into the blood, helps to maintain blood pressure and sympatheticotonus in general.

The stimulus for one of the two systems, the sympathetic, is known, namely, adrenalin, though it is probably not the only one. But we do not know its antagonist. Nor do we know the stimulus for the vagal system. The thyroid contains some sympathicomimetic substances. They differ, however, from adrenalin in their action. In pituitrin we have a blood-pressure-raising substance that differs from adrenalin.

II. *Internal Secretions Originating Within the Digestive Apparatus Itself.*

A. The Pancreatic Hormone.

The pancreas does not, like most of the other endocrine glands, furnish an internal secretion exclusively. On the contrary, as every one knows, it is one of the most important of the glands supplying external secretion. This external pancreatic secretion was the subject of investigation for a long time before clinical observation, together with experiment as to the total extirpation of the pancreas, suggested the presence of an internal secretion as well. In 1889 von Mering and Minkowski, by removal of the pancreas, produced an experimental diabetes, resembling the spontaneous affection in all essentials. This led them to conclude that after removal of the pancreas some substance is accumulated in the body that is detrimental to carbohydrate metabolism, or else that some substance or function that normally serves to promote carbohydrate metabolism is lacking. This substance is the pancreatic hormone. So far, however, it has not been isolated, and the hope of obtaining a substance that can supply the deficiency associated with a diseased or inadequate organ, as has been done in the case of the thyroid, is not yet realized. Obviously, the pancreatic hormone is produced only as it is required and immediately utilized; there is no storing-up of reserves.

The existence of an internal pancreatic secretion was actually demonstrated by Forschbach in 1908. Eppinger and Hess, as well as Falta and Ruedinger, have shown that the thyroid exercises a certain influence upon carbohydrate metabolism that is apparently brought to bear through the agency of the pancreas. From their

experiments it would seem that while the action of the thyroid is opposed to the action of the pancreatic secretion, that of the parathyroids is favorable to it.

Laguesse in 1893 expressed the opinion that the so-called islands of Langerhans in the pancreas might be the seat of the internal pancreatic secretion. With regard to the relation between the islands and the acini, however, there seems to be no unanimity of opinion. According to one view the islands have nothing to do with the acini, although they are connected anatomically with the rest of the pancreatic tissue. According to another, the islands are an early stage of the acini. MacCullum in 1911 stated that the weight of evidence favored the view that the adrenal secretion could, in some cases, stir up the tissue of the islands to set free secretion into the circulation or to mobilize carbohydrates, but whether it does so by inhibiting the action of the pancreas seems to be as yet undetermined.

Von Noorden first advocated the view that in every case of real diabetes there is a functional breakdown of the pancreas. A pancreas may appear quite normal on macroscopical examination and may possess a normal apparatus for external secretion, while at the same time there are grave changes throughout the interdependent system of islands. Characteristic histological changes will be found, he considers, in almost 90 per cent. of severe cases of diabetes. In milder forms such changes are present in 40 to 65 per cent. There must also be functional disturbances of the internal pancreatic secretion, connected with inhibitory proceedings from other endocrine glands. Opie's careful studies indicate that the intensity of diabetes is inversely in proportion to the total quantity of Langerhans' islands able to carry on their normal function. And, if inadequacy of the islands is recognized as the cause of deficiency in the pancreatic secretion and, in the long run, of diabetes, it can be brought about as von Noorden emphasizes by two wholly different conditions: one a disease of the islands caused by disturbance of their environment; the other a specific disease occurring independently of their surrounding tissue. In the second class of cases there are two conditions of importance. First, congenital atony of the islands; second, acquired atony of the islands system. As regards congenital atony it would appear that the pancreatic island system is sometimes so predisposed to atony that it cannot respond to

the demands made upon it under any conditions. In other cases, there is sufficient capability for resistance to protect the person, as long as no great amount of wear and tear is put upon the organism. The greater the load it has to carry the more considerable is the consumption of carbohydrates and of proteins. "If," says von Noorden, "in hereditary tendency to diabetes, we advise moderation in the use of carbohydrates and fats and the incorporation of as much as possible of the requisite energy in the shape of proteins, we shall, in the most rational way, transfer a verified axiom of the treatment of diabetes to the prophylaxis of the disease." In acquired atony, it would appear that some special dyscrasia is necessary to produce the development of diabetes. Infectious diseases, in von Noorden's opinion, are the chief factors, by producing lesions in the parenchyma of the islands, there being, he thinks, a specific parenchymatous lesion of them analogous to nephritis after scarlet fever. Recently the lesions in the islands have been carefully studied by Allen of the Rockefeller Hospital.

B. The Duodeno-Jejunal Hormone (Secretion).

The existence of a hormone formed in the alimentary tract was definitely established by Bayliss and Starling in 1902. The secretion of the pancreatic juice begins as soon as the acid chyme enters the duodenum. It was thought at first that the secretion was induced by the acid, stimulating nerve endings in the duodenum, but Bayliss and Starling discovered that it was elaborated just the same if acids were introduced into the lumen of a coil of the duodenum, freed from all nervous connections. The effect of the acid became less and less, the lower down it was introduced into the intestine, until, about two feet above the ileocecal valve it ceased to act altogether. Moreover, if acid was introduced into the blood-stream, it had no effect, suggesting that it acts upon something in the mucosa of the intestine, a fact established by a second experiment of Bayliss and Starling. They prepared an extract by treating mucosa scraped from the upper part of the small intestine with HCl, and they found that, when this was injected into the veins, it provoked a more immediate and profuse secretion of pancreatic juice than could be achieved in any other way, showing that the acid excites the formation of some substance in the intestinal mucosa, that is carried by the blood-

stream to the pancreas, stimulating it, in its turn, to secretion. To the substance resulting from the action of the acid upon the mucous membrane they gave the name *secretin,* while its precursor found in the mucosa, they called *prosecretin.* Secretin is not a ferment because it withstands boiling, but its action from the chemical standpoint is still unknown, in spite of much investigation. It corresponds to the other hormones in being of small molecular weight.

It has not been found possible to make any therapeutic use of secretin, as was hoped at first might be done, because, in the first place, it cannot be extracted from the alimentary canal, but must be manufactured within the intestinal mucosa; in the second place, if it is injected into the blood-stream when there is no food in the duodenum, it causes a rapid secretion of pancreatic juice, resulting in a dangerous self-digestion of the walls, accompanied by enteritis. At present, therefore, we can regulate secretion only through the acidity of the gastric juice. If the gastric secretion is inadequate, there will be an inadequate pancreatic secretion. Hyperchlorhydria, on the other hand, tends to exhaust the pancreas. Pancreatic inadequacy, however, tends to excite some degree of hyperchlorhydria, because the normal neutral mechanism is partially in abeyance, thus establishing a vicious circle. It has not yet been determined whether secretin is a stimulant of the internal as well as of the external pancreatic secretion. Some observers have suggested that there is an absence of prosecretin in the intestinal mucosa in diabetes, but it has certainly been found present in abundance in some cases of diabetic coma. Bayliss and Starling established the fact that secretin causes a slight secretion of bile.

C. The Hormone of the Pyloric Glands (Gastrin).

The fact that there is a striking difference between the histological structure of the glands of the fundus and those of the pylorus would seem to suggest that there is a difference in their function, but this difference was not actually established until Edkins applied Bayliss and Starling's experiments to the stomach. Edkins made an extract of the pyloric mucous membrane from the stomach of a fasting cat and injected it into the circulation of another fasting animal. A secretion of gastric juice containing both HCl and pepsin followed. Meat extracts, containing

creatin yielded even better results, while similar effects of the same nature, though less marked, were produced by extracts made with boiling water, glucose, or peptone. Extracts prepared in the same way from other glands of the stomach excited no secretion. Edkins also found that if the pyloric end of the stomach was divided from the fundus by means of a tampon, the injection of pyloric extract into the circulation caused a flow of gastric juice on the fundus side of the divisions, but not upon that of the pylorus. It is believed, therefore, that the extracts just described stimulate the formation of a gastric substance that, passing through the circulation, excites the secretion of gastric juice by the glands at the fundus of the stomach. The substance was called *gastrin* by Edkins and *gastric secretin* by Bayliss and Starling.

D. The Internal Secretion of the Liver.

It seems doubtful whether any of the substances poured into the blood stream by way of the hepatic vein really come within Starling's definition of a hormone, as a chemical messenger that, carried by the blood-stream, excites some other glands into activity. There are, however, three substances poured into the blood by way of the hepatic vein, that call for consideration—namely, (*a*) antithrombin; (*b*) urea; and (*c*) glucose.

(*a*) *Antithrombin.*—Delezenne described some experiments that indicate that the liver produces a substance that tends to prevent clotting of blood. This substance is now known as antithrombin.

(*b*) *Urea.*—It has long been known that the liver is the principal, though probably not the only site for the formation of urea, but it has only recently been established that urea is in great part formed from food and that the products of protein digestion are thrown into the portal circulation mainly, if not entirely, as amino-acids. From these amino-acids the liver, apparently, selects those substances needed for the immediate nutrition of the tissues, while it deprives the remainder of their amino-groups, converting them into urea. The carbon residue, we may presume, is utilized as an immediate source of energy. The urea circulating in the blood acts as a diuretic when it reaches the kidneys by which it is excreted.

(*c*) *Glucose.*—The liver and the muscles are the great store-

house for glycogen, the glucose abstracted during digestion being synthetized in the liver to glycogen. This glucose is given over to the blood gradually in small amounts, as it is needed, being mobilized from its depot by means of amylase, produced, apparently, under the influence of sympathetic innervation stimulated in its turn, by the epinephrin circulating in the blood. The normal liver can convert fructose (levulose) first, into glucose and then into glycogen. In hepatic insufficiency this function of the liver may suffer. If glucose is given over to the blood too rapidly by the liver, it will cause a glycosuria.

Conclusion.

From this summary of the relations existing between the endocrine glands and the digestive system, the outstanding features would appear to be—

1. The diarrhea and accelerated metabolism in Graves' disease.
2. The constipation and retarded metabolism of myxedema.
3. The enamel defects and disturbance of calcium excretion in parathyroid insufficiency and the relation of gastric and duodenal dilatation to tetany.
4. The large medial incisors and long intestine in status thymo-lymphaticus.
5. The relation of the anterior lobe of the hypophysis cerebri to obesity and splanchnomegaly and of the pars intermedia to diabetes insipidus and its accompanying thirst.
6. The relation of the internal secretion of the pancreas and of the secretions of the chromaffin system to the mobilization of glucose.
7. The hormonic significance of certain substances (secretin, gastrin, antithrombin, etc.) produced within the digestive tract itself.
8. The connection of the endocrine glands with the glands and musculature of the digestive tract in two ways: (*a*) by a chemical route and (*b*) by neutral pathways.

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Annex